FURTHER ANALYSES OF THE ROLE OF CONFOUNDING VARIABLES IN EPIDEMIOLOGIC STUDIES OF ENVIRONMENTAL TOBACCO SMOKE AND THE RESPIRATORY SYSTEM IN SCHOOL-AGE CHILDREN.

RAPHAEL J. WITORSCH[A], JOSEPH M. WU[B], RONALD D. HOOD[C], PHILIP WITORSCH[D]

[A] Medical College of Virginia, Virginia Commonwealth University, Richmond, VA, USA

[B] New York Medical College, Valhalla, NY, USA

[C] University of Alabama, Tuscaloosa, AL, USA

[D] The George Washington University Medical Center, Washington, DC, USA

Key Words: Respiratory disease in children, Pulmonary function, Environmental tobacco smoke (ETS), Parental Smoking, Respiratory infection, Asthma, Epidemiology, Confounding variables

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ABSTRACT

A series of analyses that we have conducted to date reveal little to no consistency from study to study in the association between parental/household smoking and specific respiratory endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) or pulmonary function parameters (such as FEV_1, FEF_{25-75}, and $Vmax_{50}$) in school age or older children. We have suggested that these inconsistencies could reflect variability in the potential confounders that were considered in the studies in question. Accordingly, we have been examining the extent to which 21 predetermined potential confounding variables were addressed in the 45 clinical endpoint and 38 pulmonary function endpoint studies in question. A previous report

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examined 5 of the variables, the current report pertains to the remaining 16. This analysis reveals that there is a wide variation in the criteria used for several of the confounders under examination, most notably family size, location of residence and of the subject, active smoking, outdoor pollution, dampness and cold, type of heating/air conditioning, and quality of housing. Selected confounders were found to be consistently associated with increased prevalence of respiratory symptoms and disease (male gender), increased pulmonary function (age, male gender) or decreased pulmonary function (active smoking, location of residence). With regard to associations between clinical and pulmonary function endpoints and the remaining confounders examined here, associations were either not observed, of an uncertain nature, or could not be determined. The lack of standardization in the treatment of confounding variables, as well as the apparent influence of certain of these factors, could be responsible for the inconsistency from study to study of the association between parental/household smoking and respiratory clinical and pulmonary function endpoints in school-age and older children.

INTRODUCTION

We recently reported an updated and expanded analytical review of the literature pertaining to the relationship between parental/household smoking (as a surrogate for ETS exposure) and the respiratory system of school-age or older children, which involved 45 clinical endpoint studies and 38 pulmonary function endpoint studies [1]. As in our earlier analyses that had been done on a smaller, more limited database [2,3], this recent analysis indicated little to no consistency from study to study in the association between this surrogate for ETS exposure and specific respiratory endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) and such pulmonary function parameters as FEV_1, FEF_{25-75}, and $Vmax_{50}$ [1].

Since potential confounding variables (i.e., other factors that might co-vary with the independent variable) are recognized as important factors that can affect the outcome of an epidemiologic study [4-6], we have suggested that this lack of consistency could reflect the variability with which potential confounders were considered in the studies in question [1-3]. We have also suggested that the lack of verification by physician examination or medical records of parental responses to questionnaires regarding specific respiratory symptoms and diseases could contribute to inconsistencies observed from study to study with regard to clinical endpoints [1-3].

As a result of these considerations, we recently initiated further analyses to determine the extent to which 21 pre-determined confounding variables were addressed in the 45 clinical endpoint and 38 pulmonary function endpoint studies in question, as well as determining the frequency with which clinical endpoints were verified (i.e., by medical examination or medical records) in the former. An initial report of this further analysis dealt with the frequency with which these clinical endpoints were verified, the frequency and consistency with

which these 21 confounders were
criteria and effects) pertaining to 5
omic status, gas stove usage, othe
history, and subject's personal healt
an analysis of the 16 remaining con

MATERIALS

The 45 clinical endpoint studies a
under examination correspond to th
The 21 potential confounders under
variables considered in the paper
studies, as well as from factors that
direct or indirect effect on the resp
designated with an asterisk were co
remainder are considered here.

Table 1. Potential Confounders Co
Household Smoking and
of School-Age and Older

1. Socioeconomic status*
2. Gas stove usage*
3. Family health history*
4. Subject's personal health history*
5. Infant feeding (breast vs. bottle)
6. Outdoor pollution
7. Indoor pollution (other than gas stove us
8. Day care use
9. Family size
10. Animal exposures
11. Stress

* Potential confounders considered in p

As described previously [7], a pr
relevant information from each
confounders were regarded as hav
criteria were fulfilled: 1) the auth
be homogeneous with regard to a
parental/household smoking) and

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which these 21 confounders were considered. and specific details (such as criteria and effects) pertaining to 5 individual confounders, namely socioeconomic status, gas stove usage, other forms of indoor pollution, family health history, and subject's personal health history [7]. The current report deals with an analysis of the 16 remaining confounding variables.

MATERIALS AND METHODS

The 45 clinical endpoint studies and 38 pulmonary function endpoint studies under examination correspond to those reviewed in previous reports [1-3,7-75]. The 21 potential confounders under examination (Table 1) were derived from variables considered in the papers under review and other epidemiologic studies, as well as from factors that intuitively seemed likely to have a potential direct or indirect effect on the respiratory system. As shown in Table 1, those designated with an asterisk were considered in our previous report [7], while the remainder are considered here.

Table 1. Potential Confounders Considered in Epidemiologic Studies of Parental/Household Smoking and Respiratory Health and Pulmonary Function of School-Age and Older Children

1. Socioeconomic status*	12. Dampness and cold
2. Gas stove usage*	13. Type of heating and presence of air conditioning
3. Family health history*	14. Season
4. Subject's personal health history*	15. Occupational exposures of subject (direct or indirect)
5. Infant feeding (breast vs. bottle)	16. Quality of housing
6. Outdoor pollution	17. Nutritional status of subject
7. Indoor pollution (other than gas stove usage)*	18. Residence location
8. Day care use	19. Age of subject
9. Family size	20. Gender of subject
10. Animal exposures	21. Active smoking by subject
11. Stress	

* Potential confounders considered in previous report [7]

As described previously [7], a protocol was employed to systematically extract relevant information from each of the studies under examination. Potential confounders were regarded as having been addressed if any one of the following criteria were fulfilled: 1) the authors of the study considered the population to be homogeneous with regard to a potential confounder; 2) the exposed (e.g. to parental/household smoking) and nonexposed subjects were said to be matched

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ETS Exposure, Confounding

with regard to the potential confounder; 3) statistical adjustment was made for the potential confounder; or 4) it was regarded in the study as an independent risk factor.

The following information pertaining to potential confounding variables was tabulated: 1) what criterion (or criteria) was (were) employed for each potential confounders; 2) whether a statistically significant association was looked for between a potential confounder and an endpoint and, if so, what was the direction of this association; and 3) whether there was evidence of possible interaction between the potential confounder in question and other potential confounders (including parental/household smoking) that influenced the outcome of the study. From this tabulated information, the consistency from paper to paper relative to each item was determined.

In two instances, the Park and Kim study [34, 35] and the Stern et al. study [40, 41], basically the same data, slightly updated, was reported twice. Although each of the reports is cited, for each study the two reports are considered to represent a single study in the following tabulations.

RESULTS

Table 2. Consideration of Family Size in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease of Older Children

Published Study	Parameter	Association of Parameter(s)
Colley, 1974 [9]	number of siblings	associated with increased respiratory symptoms
Lebowitz/Burrows, 1976 [10]	family size	none reported
Said et al., 1978 [12]	number of siblings	associated with decreased prevalence of adenoidectomy and tonsillectomy
Tager et al., 1979 [15]	number of persons per room comparable in exposed & nonexposed households, controled for sibship size	NA (matched)
Weiss et al., 1980 [17]	density of persons per room	none observed for wheeze
Bonham/Wilson, 1981 [18]	number of adults in household	none observed for restricted activity due to respiratory illness of the child
Dodge, 1982 [19]	avg size of household same for exposed and nonexposed subjects	NA (matched)
Gortmaker et al., 1982 [20]	family size	none reported

Published Study	
Tashkin et al., 1984 [26]	stated evenly expos
Vogt, 1984 [27]	no. of hold
Ware et al., 1984 [28]	numb home
Fergusson/Horwood, 1985 [29]	famil
Horwood et al., 1985 [30]	famil
Burchfiel et al., 1986 [32]	numb
McConnochie/Roghmann, 1986 [33]	crow pres
Park/Kim, 1986, 1988 [34, 35]	num num
Strachan/Elton, 1986 [36]	4 or othe than
Willat, 1986 [38]	fam
Dijkstra et al., 1988 [44]	crov pos
Somerville et al., 1988 [46]	nur cro
Angioni et al., 1989 [47]	no. san inc
McConnochie/Roghmann, 1989 [50]	fan cro
Neuspeil et al., 1989 [51]	cro

A. Family Size

As shown in Table 2, seve endpoint papers that considered of persons/room; number of a as a dichotomized or continu individuals occupying the subj observed association betwee toms and/or diseases [17, 18, observing either a positive [9]

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Published Study	Parameter	Association of Parameter(s)
Tashkin et al., 1984 [26]	stated that family size was evenly distributed among exposure groups	NA (matched)
Vogt, 1984 [27]	no. of children in household	associated with decreased utilization of outpatient and inpatient care services at HMO
Ware et al., 1984 [28]	number of persons living in home	none reported
Fergusson/Horwood, 1985 [29]	family size	none reported
Horwood et al., 1985 [30]	family size	none observed for asthma
Burchfiel et al., 1986 [32]	number persons in household	none reported
McConnochie/Roghmann, 1986 [33]	crowding in household; presence of older siblings	none observed for asthma and wheezing
Park/Kim, 1986, 1988 [34, 35]	number of family members; number of siblings	none observed for coughing
Strachan/Elton, 1986 [36]	4 or more persons in family; other children in family; more than 1 person/room	none observed for wheeze, cough, respiratory illness
Willat, 1986 [38]	family density no. of siblings	none observed for sore throats
Dijkstra et al., 1988 [44]	crowding of home and possession of own bedroom	none reported
Somerville et al., 1988 [46]	number of siblings; household crowding	none reported
Angioni et al., 1989 [47]	no. of people sleeping in same room as child; crowding index (no. people per room)	none observed respiratory and nonrespiratory allergies
McConnochie/Roghmann, 1989 [50]	family size and household crowding	none observed for asthma or wheezing
Neuspeil et al., 1989 [51]	crowding in home	none observed for wheezy bronchitis

A. Family Size

As shown in Table 2, several criteria were variably employed in the 23 clinical endpoint papers that considered family size including: number of siblings; number of persons/room; number of adults in the household; crowding in the household as a dichotomized or continuous variable; presence of older siblings; and number of individuals occupying the subject's bedroom. Of the 23 studies, 10 reported no observed association between family size and prevalence of respiratory symptoms and/or diseases [17, 18, 30, 33, 34, 35, 36, 38, 47, 50, 51], while 3 studies reported observing either a positive [9] or a negative [12, 27] association. Three of these

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studies were classified as matched [15, 19, 26] and 7 studies, designated as [illegible] reported", provided no data pertaining to the presence or absence of an associa[illegible] 20, 28, 29, 32, 44, 46].

Table 3 shows that 13 pulmonary function studies employed such criteria a number of siblings, number of persons/room, and number of persons in the [illegible] as indices of family size. Seven of these studies reported no observed associa[illegible] between family size and pulmonary function [55, 61, 62, 63, 69, 70, 72], while [illegible] of the studies reported an observation of the existence of such an association. F[illegible] studies were classified as homogeneous or matched [15, 19, 26, 67] and 2 stu[illegible] reported no data relative to this issue [28, 32].

Table 3. Consideration of Family Size in Studies of Parental/Household Smoki[illegible] and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameters
Leeder et al., 1976 [55]	number of siblings	none observed for peak expiratory flow rate
Tager et al., 1979 [15]	number of persons per room comparable in exposed and nonexposed households; controlled for sibship size	NA (matched)
Ware et al., 1984 [28]	number of persons living in home	none reported
Hasselbad et al., 1981 (61)	density of people per room	none observed for $FEV_{0.5}$
Dodge, 1982 [19]	avg size of household was same for exposed and non-exposed subjects	NA (matched)
Lebowitz et al., 1982 [62]	family size	none observed for FVC, FEV_1, $Vmax_{50}$, and $Vmax_{75}$
Lebowitz et al., 1984 [63]	family size	none observed for family aggregation of pulmonary function
Tashkin et al., 1984 [26]	family size was evenly distributed among exposure groups	NA (matched)
Burchfiel et al., 1986 [32]	family size	none reported
Chen/Li, 1986 [67]	avg household residential area per capita similar in exposed and nonexposed subjects	NA (matched)
Evans et al., 1987 [69]	number of people in household, number of people per room	none observed for FEV_1
Martinez et al., 1988 [70]	number of persons in household	none observed for bronchial responsiveness
Murray/Morrison, 1988 [72]	number of siblings	none observed for baseline pulmonary function and bronchial responsiveness in asthmatics

B. Location of Residence

As shown in Table 4, 25 studie[illegible] potential confounding variable in [illegible] following criteria: proximity to regi[illegible] and definition of area as urban, sub[illegible] 13 were considered to be homoge[illegible] 36, 39, 40, 41, 42, 44, 50, 52]. F[illegible] association [14, 16, 24, 47], three r[illegible] 43], and four provided no relevant[illegible] data suggested a possible interac[illegible] pollution and parental/household[illegible]

Table 4. Consideration of Loca[illegible] Household Smoking ar[illegible] Children

Published Study	Param[illegible]
Kasuga et al., 1979 [14]	reside[illegible] proxir[illegible]
Tager et al., 1979 [15]	East [illegible] graph[illegible]
Speizer et al., 1980 [16]	Harv[illegible] (12 s[illegible] 6 citi[illegible]
Weiss et al., 1980 [17]	East [illegible] grap[illegible]
Dodge, 1982 [19]	non-[illegible] sma[illegible] size pres[illegible] sme[illegible]
Gortmaker et al., 1982 [20]	urb[illegible] (Be[illegible] sur[illegible]
Rantakallio, 1983 [22]	pla[illegible] vil[illegible]
Schenker et al., 1983 [23]	are[illegible] pr[illegible]
Charlton, 1984 [24]	in[illegible] re[illegible]

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s, designated as "none
ence of an association [10,

mployed such criteria as
of persons in the home
no observed association
3, 69, 70, 72], while none
such an association. Four
19, 26, 67] and 2 studies

ntal/Household Smoking

Association of Parameter(s)
none observed for peak expiratory flow rate
NA (matched)
reported
observed for $FEV_{0.5}$
NA (matched)
none observed for FVC, FEV, $Vmax_{50}$, and $Vmax_{75}$
none observed for family aggregation of pulmonary function
NA (matched)
none reported
NA (matched)
none observed for FEV
none observed for bronchial responsiveness
none observed for [illegible] pulmonary function [illegible] responsiveness in asthmatics

B. Location of Residence

As shown in Table 4, 25 studies that considered location of residence as a potential confounding variable in clinical endpoint studies variably used the following criteria: proximity to region of pollution; geographically defined area; and definition of area as urban, suburban, nonurban, and rural. Of these studies, 13 were considered to be homogeneous or matched [15, 17, 29, 30, 33, 34, 35, 36, 39, 40, 41, 42, 44, 50, 52]. Four of these studies reported no observed association [14, 16, 24, 47], three reported observing an association [19, 20, 31, 43], and four provided no relevant information [22, 23, 28, 54]. In one study, the data suggested a possible interaction between location of residence, outdoor pollution and parental/household smoking [14].

Table 4. Consideration of Location of Residence in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter	Association of Parameter(s)
Kasuga et al., 1979 [14]	residential area within Tokyo, proximity to highway	see Table 12 B none observed for this parameter alone
Tager et al., 1979 [15]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Speizer et al., 1980 [16]	Harvard Six Cities Study (12 separate cohorts from 6 cities)	none observed for respiratory illness before 2 years of age (not reported for other endpoints)
Weiss et al., 1980 [17]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Dodge, 1982 [19]	non-urban, all subjects from 3 small communities ranging in size from 4000 to 7312 people; presence or absence of copper smelters within community	see Table 12 B
Gortmaker et al., 1982 [20]	urban (Flint, Mich.) and rural (Bershire, Mass.) from 2 seperate survey populations	urban area associated with increased incidence of asthma
Rantakallio, 1983 [22]	place of residence (town-village-remote, village)	none reported
Schenker et al., 1983 [23]	area predominantly rural, proximity to industrial pollution	see Table 12 B
Charlton, 1984 [24]	industrial vs. non-industrial regions	none observed for prevalence of cough

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Published Study	Parameter	Association of Parameter
Ware et al., 1984 [28]	Harvard Six Cities Study (6 locations with range of outdoor air qualities); adjustment as "city-cohort" in multiple logistic regression	none reported
Fergusson/Horwood, 1985 [29]	urban region of Christchurch, New Zealand	NA (homogeneous)
Horwood et al., 1985 [30]	urban region of Christchurch, New Zealand	NA (homogeneous)
Spinaci et al, 1985 [31]	3 geographic areas within Turin, Italy	see Table 12 B
McConnochie/Roghmann, 1986 [33]	suburban Rochester, N.Y.	NA (homogeneous)
Park/Kim, 1986, 1988 [34, 35]	rural (Korea)	NA (homogeneous)
Strachan/Elton, 1986 [36]	urban area of Edinburgh, Scotland	NA (homogeneous)
O'Connor et al., 1987 [39]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all locations rural Canada but adjustment for city of residence	see Table 12 B
Tsimoyianis et al., 1987 [42]	suburban Nassau County, New York	NA (homogeneous)
Andrae et al., 1988 [43]	7 rural areas, 2 of the areas areas compared on the basis of proximity to pulp and paper plant	proximity to pulp and paper plant associated with increased bronchial hyperreactivity and allergic disease;
Dijkstra et al., 1988 [44]	rural area of southeast Netherlands	NA (homogeneous)
Angioni et al., 1989 [47]	home in inner city, suburb, and country	none observed for allergic respiratory and nonrespiratory disease
Charlton/Blair, 1989 [54]	school area	none reported
McConnochie/Roghmann, 1989 [50]	suburban Rochester, N.Y.	NA (homogeneous)
Sherman et al., 1990 [52]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)

Location of residence (geographically defined area, proximity to source of outdoor pollution, and definition of area as urban, suburban, and rural) was considered in 20 pulmonary function endpoint studies and is detailed in Table 5. Eleven of these studies were classified as homogeneous or matched [55, 57, 15, 17, 58, 59, 39, 67, 69, 42, 44]. One study reported no observed association

19] and four studies reported th
of pulmonary function [16, 60,
regarding location of residence

Table 5. Consideration of Locat
Smoking and Pulmo

Published Study	Par
Leeder et al., 1976 [55]	Har of
Tager et al., 1976 [57]	Eas ph
Tager et al., 1979 [15]	Eas ph
Weiss et al., 1980 [17]	Ea ph
Tager et al. 1983 [58]	Ea ph
Tager et al., 1985 [59]	Ea ph
O'Connor et al., 1987 [39]	Ea pl
Speizer et al. 1980 [16]	H se a b
Ware et al., 1984 [28]	H (c a i
Berkey et al., 1986 [60]	H (
Hasselbad et al., 1981 [61]	
Dodge, 1982 [19]	

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...ssociation of Parameter(s)
...one reported
NA (homogeneous)
NA (homogeneous)
see Table 12 B
NA (homogeneous)
NA (homogeneous)
NA (homogeneous)
NA (homogeneous)
see Table 12 B
NA (homogeneous)
...imity to pulp and paper associated with increased ...onchial hyperreactivity and allergic disease.
NA (homogeneous)
none observed for allergic respiratory and nonrespiratory disease
none reported
NA (homogeneous)
NA (homogeneous)

area, proximity to sour... n, suburban, and rural ... ...udies and is detailed in T... ...ogeneous or matched ... ...rted no observed ass...

[19] and four studies reported that location of residence was associated with level of pulmonary function [16, 60, 61, 31]. Four studies provided no information regarding location of residence and pulmonary function [28, 26, 40, 41, 74].

Table 5. Consideration of Location of Residence in Studies of Parental/Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameter(s)
Leeder et al., 1976 [55]	Harrow, a residential suburb of NW London	NA (homogeneous)
Tager et al., 1976 [57]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al., 1979 [15]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Weiss et al., 1980 [17]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al. 1983 [58]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Tager et al., 1985 [59]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
O'Connor et al., 1987 [39]	East Boston, Mass., a geographically defined urban area	NA (homogeneous)
Speizer et al. 1980 [16]	Harvard Six Cities Study (12 separate cohorts from 6 cities); adjustment for cohort (including both location and year of study)	cohort was associated with FEV_1 and FVC, indicating differences from city to city and year to year in these parameters
Ware et al., 1984 [28]	Harvard Six Cities Study (6 locations with range of outdoor air qualities); adjustment as "city-cohort" in multiple logistic regression	none reported
Berkey et al., 1986 [60]	Harvard Six Cities Study (corrected for 6 separate locales)	some geographic differences observed in level and growth rates of FVC and FEV_1
Hasselbad et al., 1981 [61]	33 communities from 7 metropolitan areas in different geographic locations in US; considered in analysis of covariance	accounted for the greatest amount of variation in mean $FEV_{0.75}$; see also table 13 B
Dodge, 1982 [19]	non-urban, all subjects from 3 small communities ranging in size from 4000 to 7312 people; presenceor absence of copper smelters within community	see Table 13 B none observed

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Published Study	Parameter	Association of Parameter
Tashkin et al., 1984 [26]	4 selected areas of Los Angeles County (adjusted for)	none reported
Spinaci et al., 1985 [31]	3 geographic areas [central urban (UC), peripheral (UP) and sub-urban (SU)] within Turin, Italy	see Table 13 B
Chen/Li, 1986 [67]	urban district of Shanghai	NA (homogeneous)
Evans et al., 1987 [69]	urban, 4 hospitals in New York City	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all locations, rural Canada; adjusted for city of residence	none reported
Tsimoyianis et al., 1987 [42]	suburban Nassau County, New York	NA (homogeneous)
Dijkstra et al., 1988 [44]	rural area of southeast Netherlands	NA (homogeneous)
Kauffmann et al., 1989 [74]	24 areas in 7 French cities; adjusted for town of residence	none reported

Published Study	P
Speizer et al., 1980 [16]	a
Weiss et al., 1980 [17]	r
Bonham/Wilson, 1981 [18]	
Dodge, 1982 [19]	
Gortmaker et al., 1982 [20]	
Ekwo et al., 1983 [21]	
Rantakallio, 1983 [22]	
Schenker et al., 1983 [23]	
Charlton, 1984 [24]	
Lebowitz, 1984 [25]	
Tashkin et al., 1984 [26]	
Vogt, 1984 [27]	
Ware et al., 1984 [28]	
Fergusson/Horwood, 1985 [2	
Horwood et al., 1985 [30]	
Spinaci et al, 1985 [31]	

C. Age of the Subject

Table 6. Consideration of Age of Subject in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter (ages)	Association of Parameter(s)
Cameron et al., 1969 [8]	5 or less vs. 9 or less vs. 16 or less (5 or less -16)	household smoke exposure associated with increased respiratory illness 16 or less not in other age groups
Colley, 1974 [9]	age of child (6-14)	none reported
Lebowitz/Burrows, 1976 [10]	age of child (under 15)	none reported
Schilling et al., 1977 [11]	7-15 yrs of age vs. 15-18 (7-18)	prevalence of wheeze in children associated with parental wheeze in younger children (numbers may be inadequate in older children)
Said et al., 1978 [12]	above and below 15 years of age (10-20)	none observed for adenoid-ectomy or tonsillectomy
Bland et al., 1978 [13]	all children in 1st yr of secondary school (not given)	NA (homogeneous)
Kasuga et al., 1979 [14]	none (6-11)	NA
Tager et al., 1979 [15]	none (5-9)	NA

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Association of Parameter(s)
none reported
see Table 13 B
NA (homogeneous)
NA (homogeneous)
none reported
NA (homogeneous)
NA (homogeneous)
none reported

dies of Parental/Household
d Disease in Older Children

ociation of Parameter(s)
household smoke exposure associated with increased respiratory illness 16 or less not in other age groups
none reported
none reported
prevalence of wheeze in children associated with parental wheeze in younger children (numbers may be inadequate in older children)
none observed for adenoidectomy or tonsillectomy
NA (homogeneous)
NA
NA

Published Study	Parameter	Association of Parameter(s)
Speizer et al., 1980 [16]	age at time of reporting (6-10)	none observed for infant respiratory disease
Weiss et al., 1980 [17]	none (4-10)	NA
Bonham/Wilson, 1981 [18]	under 6 vs. 6-11 vs. 12-16 yr (0-16)	none observed for restricted activity due to acute respiratory conditions
Dodge, 1982 [19]	subjects were 3rd and 4th grade children at incepuons fo the 4 yr longitudinal study (8-12)	NA (homogeneous)
Gortmaker et al., 1982 [20]	above and below 5 yrs of age (0-17)	none observed for asthma
Ekwo et al., 1983 [21]	none (6-12)	NA
Rantakallio, 1983 [22]	all subjects were the same age (14)	NA (homogeneous)
Schenker et al., 1983 [23]	5-9 yrs vs 10-14 years (5-14)	respiratory symptoms (cough, phlegm, wheeze) and chest illness more prevalent in younger children
Charlton, 1984 [24]	<11, 11-13, >14 yrs of age (8-19)	prevalence of cough decreased with increasing age
Lebowitz, 1984 [25]	none. (4-24)	NA
Tashkin et al., 1984 [26]	age of child (7-17)	none reported
Vogt, 1984 [27]	age of child (0-5 vs. 6-11 vs. 12-18 yrs) (0-18)	as child ages outpatient service utilization (primarily for upper respiratory infection), as well as inpatient care, declines
Ware et al., 1984 [28]	age of children (6-10)	prevalence of respiratory illnesses higher in younger children
Fergusson/Horwood, 1985 [29]	birth cohort compared at intervals of 2yrs (0-6)	prevalence of respiratory symptoms and illness decreases as age of the child increases; association with maternal smoking disappears after 2 years of age
Horwood et al., 1985 [30]	birth cohort compared at yearly intervals (0-6)	cumulative rates of asthma (per 100 children) increased with age as the number of risk factors increased
Speizer et al, 1985 [31]	age of child (11)[a]	none reported

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Published Study	Parameter	Association of Parameter
Burchfiel et al., 1986 [32]	0-4yr vs. 9yr vs. 10-14yr vs. 15-19 yr (0-19)	prevalence of phlegm and chest colds tend as age increases but not statistically significant; no consistent age association for cough, asthma, and bronchitis
McConnochie/Roghmann, 1986 [33]	mean age 8.4 yr (6-10)	NA (homogeneous)
Park/Kim, 1986, 1988 [34, 35]	child's age (under 5 vs. 6-11 vs. 12-14 yr) (0-14)	incidence coughing decreases with increasing age
Strachan/Elton, 1986 [36]	children approximately the same age (7-8)	NA (homogeneous)
Teculescu et al., 1986 [37]	exposed child matched for age with nonexposed child (10-16)	NA (matched)
Willat, 1986 [38]	age of child (2-15)	older children had a higher prevalence of sore throats
O'Connor et al., 1987 [39]	age of subjects matched for exposed and nonexposed non-asthmatic and asthmatic subjects (6-21)	NA (matched)
Stern et al., 1987, 1989 [40, 41]	none (7-12)	NA
Tsumoyianis et al., 1987 [42]	exposed and nonexposed matched for age (12-17)	NA (matched)
Andrae et al., 1988 [43]	6 mos-7 yr vs 8-16 yr (0.5-16)	outdoor pollution associated with increased incidence of asthma and coughing in older group of children
Dijkstra et al., 1988 [44]	age of child (6-12)	none reported
Moreno et al., 1988 [45]	none (8-13)	NA
Somerville et al., 1988 [46]	none (5-11)	NA
Angioni et al., 1989 [47]	age of subject (6,7,8,9,10, and 10+ yr) (6-10+)	none observed for respiratory and nonrespiratory allergic disease
Berwick et al., 1989 [48]	above and below 7 yrs of age (5-13)	children below age of 7 yr exhibit increased incidence lower respiratory symptoms when exposed to 30 ug/m^3 NO_2
Chan et al., 1989 [49]	all children same age (7)	NA (homogeneous)
Charlton/Blair, 1989 [54]	all children same age (12-13)	NA (homogeneous)

Published Study	Pa
McConnochie/Roghmann, 1989 [50]	cc 8 (((
Neuspeil et al., 1989 [51]	b s:
Sherman et al., 1990 [52]	b a
Strachan et al., 1990 [53]	a
[a]Average age	

As shown in Table 6, a w
employed in the 45 clinical
smoking. 38 studies attempt
variable. In 12 of these stu
homogeneous or matched
studies reported no significa
and clinical endpoints [12,
that the prevalence of respi
got older within a study pop
studies suggested an interac
such as household smoke e
and subject's health history
association, i.e., that risk of
[30, 38, 43]. Five of these
regarding any association

As in the case of the cl
comparisons and age range
considered age of the subj
the majority of these stu
pulmonary function (Table
ous for age in 10 studies [5
reported no observed assc
age and some parameter
66, 32, 67, 74] that indicat
aged. Several studies sug
other factors with regard to
parental/household smok
gender [64, 66] and sub
provided no direct inform
and pulmonary function [5

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Association of Parameter(s)
prevalence of phlegm, wheeze, and chest colds tend to decrease as age increases but generally not statistically significant; no consistent age association for cough, asthma, and bronchitis
NA (homogeneous)
incidence coughing decreased with increasing age.
NA (homogeneous)
NA (matched)
older children had a higher prevalence of sore throats
NA (matched)
matched)
outdoor pollution associated with increased incidence of asthma and coughing in older group of children none reported
NA
NA
none observed for respiratory and nonrespiratory allergic disease
children below age of [illegible] exhibit increased incidence lower respiratory symptoms when exposed to 30 ug m
NA (homogeneous)
NA (homogeneous)

Published Study	Parameter	Association of Parameter(s)
McConnochie/Roghmann, 1989 [50]	cohort examined at mean age 8 yrs with mean age 13 yrs (6-10 and 11-15)	bronchiolitis history is a risk factor for wheeze and asthma at age 8 but not 13 yrs
Neuspeil et al., 1989 [51]	birth cohort examined at same age (10 yrs)	NA (homogeneous)
Sherman et al., 1990 [52]	below and above 10 years of age (5-22)	none observed for first occurrence of asthma
Strachan et al., 1990 [53]	all children same age (6.5-7.5)	NA (homogeneous)
*Average age		

As shown in Table 6, a wide variety of age comparisons and age ranges were employed in the 45 clinical endpoint studies pertaining to household/parental smoking. 38 studies attempted to control for age of the subjects as a confounding variable. In 12 of these studies, age of the subject was considered either to be homogeneous or matched [13, 19, 22, 33, 36, 37, 39, 42, 49, 54, 51, 53]. Seven studies reported no significant observed association between age of the subject and clinical endpoints [12, 16, 18, 20, 32, 47, 52]. Nine of the studies indicated that the prevalence of respiratory symptoms and illness decreased as the child got older within a study population [11, 23, 24, 27, 28, 29, 34, 35, 48, 50]. Several studies suggested an interaction between age of the subject and other variables, such as household smoke exposure [8], family history [11], indoor pollution [48] and subject's health history [50]. Three studies reported observing a converse association, i.e., that risk of respiratory illness increased with age of the subject [30, 38, 43]. Five of these studies [9, 10, 26, 31, 44] provided no information regarding any association between age of the subject and clinical endpoints.

As in the case of the clinical endpoint studies, there were a variety of age comparisons and age ranges in the 37 pulmonary function endpoint studies that considered age of the subject as a potential confounding variable, although in the majority of these studies this involved an age adjustment relative to pulmonary function (Table 7). Pulmonary function was matched or homogeneous for age in 10 studies [55, 56, 39, 68, 37, 42, 70, 72, 73, 53]. None of the studies reported no observed association. 12 studies reported an association between age and some parameter of pulmonary function [11, 58, 59, 60, 61, 19, 64, 26, 66, 32, 67, 74] that indicated increases in the level of performance as the child aged. Several studies suggested interactions between age of the subject and other factors with regard to pulmonary function, such as active smoking [59, 64], parental/household smoking [64, 75], gender and maternal smoking [61, 26, 71], gender [64, 66] and subject's personal health history [64]. Sixteen studies provided no direct information on any association between age of the subject and pulmonary function [57, 15, 17, 16, 28, 21, 62, 25, 63, 65, 31, 40, 41, 44, 69, 71, 75].

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Table 7. Consideration of Age of Subject in Studies of Parental Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter (ages)	Association of Parameter
Leeder et al., 1976 [55]	all children same age (5)	NA (homogeneous)
Schilling et al., 1977 [11]	adjusted for age; age considered in multiple regression analysis (7-18)	age (as well as weight and height) major contributor to variance
Yarnell/St. Leger, 1979 [56]	none (7-18)	NA
Tager et al., 1976 [57]	adjusted for age (5-31)	none reported
Tager et al., 1979 [15]	adjusted for age (5-19)	none reported
Weiss et al., 1980 [17]	adjusted for age (5-10)	none reported
Tager et al., 1983 [58]	adjusted for age; age considered in autoregressive model (4-28)	age of subject had negative influence on change in FEV_1 over a one year period
Tager et al., 1985 [59]	adjusted for age; age considered in autoregresssive model (5-19)	age-dependent FEV_1 growth curve is sigmoid between 5-20 years; decrement in FEV_1 and FEF_{25-75} associated with smoking most pronounced in older children (>15 yrs)
O'Connor et al., 1987 [39]	age of subjects not significantly different for exposed and nonexposed (as well as asthmatic and nonasthmatic) subjects (6-21)	NA (matched)
Speizer et al. 1980 [16]	adjusted for age (6-10)	none reported
Ware et al., 1984 [28]	adjusted for age (6-9)	none reported
Berkey et al., 1986 [60]	adjusted for age (6-10)	unadjusted FEV_1 and FVC increase with age from 6-10 years
Hasselbad et al., 1981 [61]	function adjusted for age; compared at 6-9 vs. 9-13 yrs (6-13)	$FEV_{0.75}$ increased in older children; according to authors maternal smoking produced a larger decrement in $FEV_{0.75}$ of older boys than younger boys and older and younger girls
Dodge, 1982 [19]	subjects were 3rd and 4th grade children at inception of this 4 year longitudinal study; lung growth adjusted for age of subject (8-12)	FEV_1 increases as child ages

Published Study	Parame
Ekwo et al., 1983 [21]	age of regres
Lebowitz et al., 1982 [62]	adjust
Lebowitz, 1984 [25]	adjust
Lebowitz et al., 1984 [63]	adjust
Lebowitz et al., 1987 [64]	age o regre
Lebowitz/Holberg, 1987 [65]	adj
Tashkin et al., 1984 [26]	adj con 17
Vedal et al., 1984 [66]	ad
Spinaci et al., 1985 [31]	a
Burchfiel et al., 1986 [32]	a f 1

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of Parental/Household Children

ssociation of Parameter(s)
A (homogeneous)
ge (as well as weight and veight and height) major contributor to variance
A
one reported
one reported
one reported
age of subject had negative influence on change in FEV_1 over a one year period
age-dependent FEV_1 growth curve is sigmoid between 5-20 years; decrement in FEV_1 and FEF_{25-75} associated with smoking most pronounced in older children (>15 yrs)
N atched)
none reported
none reported
unadjusted FEV_1 and FVC increase with age from 6-1 years
$FEV_{0.75}$ increased in older children; according to author maternal smoking produced a larger decrement in FEV .. of older boys than younger boys and older and younger girls
FEV_1 increases as child ages

Published Study	Parameter (ages)	Association of Parameter(s)
Ekwo et al., 1983 [21]	age of child considered in regression analysis (6-12)	none reported
Lebowitz et al., 1982 [62]	adjusted for age (>6)	none reported
Lebowitz, 1984 [25]	adjusted for age (4-24)	none reported
Lebowitz et al., 1984 [63]	adjusted for age (13.5)[a]	none reported
Lebowitz et al., 1987 [64]	age of child considered in regression analysis (5.5-25)	FEV_1 exhibits curvilinear relationship with age and height together; age-sex interaction exhibited for $Vmax_{50}$/FVC (higher in females aged 13-25 yr); history of AOD associated with age-dependent loss of $Vmax_{50}$; earlier onset of asthma (<5 yr) associated with greater decrements in $Vmax_{50}$; maternal smoking associated with significantly increased FVC in older age groups, smoking associated with greater decrements of function of older (15-25yr) subjects.
Lebowitz/Holberg, 1987 [65]	adjusted for age (5.5-25)	none reported
Tashkin et al., 1984 [26]	adjusted for age, function compared at 7-11 vs 12-17 yr (7-17)	pulmonary function elevated in older group of males and females, maternal smoking associated with decreases of selected functional parameters in younger males (Vmax, V_{25}, V_{50}) and older females (FEF_{25-75}, V_{50}, V_{75})
Vedal et al., 1984 [66]	adjusted for age (5-14)	age was a predictor of all functional measures (FVC, $FEV_{0.75}$, FEF_{25-75}, $Vmax_{75}$, $Vmax_{50}$); a significant interaction found between age and sex for all measures except FVC (flow rates increased in girls with age relative to boys)
Spinaci et al., 1985 [31]	age of subject (11)[a]	none reported
Burchfiel et al., 1986 [32]	adjusted for age; compared function at 10-14 vs. 15-19 yrs (10-19)	older group of children had higher levels of FEV_1, FVC, $Vmax_{50}$

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Published Study	Parameter (ages)	Association of Parameter
Chen/Li, 1986 [67]	age of child considered as a variable in regression analysis (8-16)	FVC associated with age; none reported for FEV_1, MMEF, $FEF_{62.5-87.5}$
Murray/Morrison, 1986 [68]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age (7-17)	NA (matched)
Teculescu et al., 1986 [37]	exposed and nonexposed subjects matched for age (10-16)	NA (matched)
Evans et al., 1987 [69]	age of child considered in multiple regresson analysis (4-17)	none reported
Stern et al., 1987, 1989 [40, 41]	adjusted for age (7-12)	none reported
Tsimoyianus et al., 1987 [42]	exposed and nonexposed subjects matched for age (12-17)	NA (matched)
Dijkstra et al., 1988 [44]	adjusted for age (6-12)	none reported
Martinez et al., 1988 [70]	all children same age (9)	NA (homogeneous)
Masi et al., 1988 [71]	age of subject considered in regression analysis (13-36)	duration of ETS exposure at home (persons X years) associated decreased FEF_{25-75} and $Vmax_{50}$ in males, ETS expo-in men before 17 years of age associated with decreased FEF_{25-75}
Murray/Morrison, 1988 [72]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age (7-17)	NA (matched)
Chan et al., 1989 [73]	all children same age (7)	NA (homogeneous)
Kauffmann et al., 1989 [74]	adjusted for age	(6-10) age related patterns of FEV_1, and FEF_{25-75} observed
Murray/Morrison, 1989 [75]	exposed and nonexposed asthmatic children comparable for age; function adjusted for age; compared function at 7-11, and 12-17 yrs (7-17)	in older age group maternal smoking associated with decreased FEV_1, FEF_{25-75} and PC_{20}, not FVC
Strachan et al., 1990 [53]	all children same age (6.5-7.5)	NA (homogeneous)

*Average age

E. Gender of Subject

As shown in Table 8, 32 clinical endpoint studies considered gender of subject as a confounding variable. Of these, 2 studies were matched for gender [8, 39].

Ten studies reported no observed as
clinical endpoints [13, 15, 17, 20, 24,
that the prevalence of some respi
exceeded that in females [11, 12, 16,
one study reported that the pre
predominated in females [11]. The r
between gender and parental smok
endpoint was observed only in chi
there was no consistency as to whe
male or female. One study also st
parental history of asthma and atop
pertaining to any association betw
44, 45].

Table 8. Consideration of Genc
Household Smoking an
Children

Published Study	Parame
Cameron et al., 1969 [8]	no sign in exp
Schilling et al., 1977 [11]	gende
Said et al., 1978 [12]	gende
Bland et al., 1978 [13]	gende
Tager et al., 1979 [15]	genc
Speizer et al., 1980 [16]	genc
Weiss et al., 1980 [17]	genc

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	Association of Parameter(s)
	FVC associated with age; none reported for FEV_1, MMEF, $FEF_{62.5\text{-}50\%}$
or	NA (matched)
ub-)	NA (matched)
	none reported
	none reported
ub- ")	NA (matched)
	none reported
	NA (homogeneous)
n	duration of ETS exposure at home (persons X years) associated decreased $FEF_{25\text{-}75}$ and $Vmax_{50}$ in males; ETS expo-in men before 17 years f age associated with ecreased $FEF_{25\text{-}75}$
asth- for	NA (matched)
	NA (homogeneous)
	(6-10) age related patterns of FEV_1, and $FEF_{25\text{-}75}$ observed
asth- e	in older age group maternal smoking associated with decreased FEV_1, $FEI_{...}$ and PC_{20}, not FVC
n 7)	
-7.5)	NA (homogeneous

ies considered gender not sub-
ere matched for gender

Ten studies reported no observed association between gender of the subject and clinical endpoints [13, 15, 17, 20, 24, 26, 27, 38, 47, 49]. Fourteen studies reported that the prevalence of some respiratory symptoms and/or diseases in males exceeded that in females [11, 12, 16, 23, 28, 30, 31, 32, 33, 46, 54, 50, 51, 52], while one study reported that the prevalence of certain respiratory conditions predominated in females [11]. The results of four studies suggested an interaction between gender and parental smoking, whereby the association with a particular endpoint was observed only in children of one sex [13, 32, 37, 42]. However, there was no consistency as to whether the gender affected in these studies was male or female. One study also suggested an interaction between gender and parental history of asthma and atopy [52]. Four studies provided no information pertaining to any association between clinical endpoints and gender [29, 34, 35, 44, 45].

Table 8. Consideration of Gender of the Subject in Studies of Parental/ Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter	Association of Parameter(s)
Cameron et al., 1969 [8]	no significant gender difference in exposed vs. non-exposed	NA (matched)
Schilling et al., 1977 [11]	gender	association between a particular parental illness (bronchitis, pneumonia, and asthma) and wheeze in children influenced by gender of the child
Said et al., 1978 [12]	gender	adenoidectomy or tonsillectomy in boys>girls
Bland et al., 1978 [13]	gender	no gender differences observed for cough and breathlessness, parental smoking associated with morning cough in girls not boys
Tager et al., 1979 [15]	gender	none observed for respiratory illness and isolated cough
Speizer et al., 1980 [16]	gender	respiratory disease in males>females
Weiss et al., 1980 [17]	gender	none observed for acute respiratory illnesses (croup, bronchiolitis, bronchitis, pneumonia), atopy (hay fever, asthma), and chronic symptoms (cough/phlegm, symptoms)

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Published Study	Parameter (ages)	Association of Parameter
Gortmaker et al., 1982 [20]	gender considered in logistic regression analysis	none observed for asthma
Schenker et al., 1983 [23]	gender considered in multple logistic regression	male gender risk factor for cough/phlegm, wheeze and asthma
Charlton, 1984 [24]	gender	none observed for cough
Tashkin et al., 1984 [26]	gender	none observed for respiratory symptoms
Vogt, 1984 [27]	gender considered in multiple regression	none observed for inpatient and outpatient care
Ware et al., 1984 [28]	gender	boys had higher respiratory illness and symptom than girls
Fergusson/Horwood, 1985 [29] Horwood et al., 1985 [30]	adjusted for gender gender	none reported prevalence of asthma in boys>girls; risk factors for asthma in boys>girls
Spinaci et al. 1985 [31]	gender	prevalence of wheezing, shortness of breath and asthma in boys>girls
Burchfiel et al., 1986 [32]	gender	prevalence of phlegm, wheeze, asthma, and chest colds greater in males than females (at least in one of the age groups tested);gender differences in conditions associated with parental smoking (phlegm, wheeze, asthma, chest colds in males vs. wheeze, bronchitis, chest colds in females)
McConnochie/Roghmann 1986 [33]	gender considered in bivariate and multivariate analyses	male sex associated with wheeze but not asthma in children aged 6-10 yrs
Park/Kim, 1986, 1988 [34, 35]	gender considered in multiple logistic regression	none reported
Teculescu et al., 1986 [37]	each subject matched for gender	association between parental smoking and cough primarily in boys
Willat, 1986 [38]	gender	none observed for sore throat
O'Connor et al., 1987 [39]	gender of subjects not significantly different for exposed and nonexposed non-asthmatic and asthmatic subjects	NA (matched)

Published Study	Parameter
Tsumoyianis et al.1987 [42]	gender
Dijkstra et al., 1988 [44]	ORs adju
Moreno et al., 1988 [45]	gender
Somerville et al., 1988 [46]	gender
Angioni et al., 1989 [47]	gender
Chan et al., 1989 [49]	gender
Charlton/Blair, 1989 [54]	gender
McConnochie/Roghmann, 1989 [50]	gender and m
Neuspeil et al., 1989 [51]	gende logist
Sherman et al., 1990 [52]	gende analy

Table 9 shows that 36 of considered gender. In the ma in certain analyses, adjusted f gender [65] and 2 studies were compared pulmonary functio levels of some parameters in reported higher levels of cert although reporting that gende specific information [73].

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Association of Parameter(s)
none observed for asthma
male gender risk factor for cough, phlegm, wheeze, and asthma
none observed for cough
none observed for respiratory symptoms
none observed for inpatient and outpatient care
boys had higher respiratory illness and symptom than girls
none reported
prevalence of asthma in boys>girls; risk factors for asthma in boys>girls
prevalence of wheezing, shortness of breath and asthma in boys>girls
alence of phlegm, wheeze, ..hma, and chest colds greater in males than females (at least in one of the age groups tested); gender differences in conditions associated with parental smoking (phlegm, wheeze, asthma, chest colds in males vs. wheeze, bronchitis, chest colds in females)
male sex associated with wheeze but not asthma in children aged 6-10 yrs
none reported
association between parental smoking and cough prevalence in boys
none observed for sore th...
NA (matched

Published Study	Parameter (ages)	Association of Parameter(s)
Tsumoyianis et al.1987 [42]	gender	association between ETS exposure and abnormal FEF_{25-75} or cough statistically significant in girls but not boys
Dijkstra et al., 1988 [44]	ORs adjusted for gender	none reported
Moreno et al., 1988 [45]	gender	none reported
Somerville et al., 1988 [46]	gender	prevalence of wheezing, bronchitis, asthma, and cough in boys > girls
Angioni et al., 1989 [47]	gender	none observed for respiratory and nonrespiratory allergies
Chan et al., 1989 [49]	gender	none observed for wheeze and cough
Charlton/Blair, 1989 [54]	gender	absence from school in boys > girls
McConnochie/Roghmann, 1989 [50]	gender considered in crude and multivariate analyses	male sex associated with wheezing and asthma at age 13
Neuspeil et al., 1989 [51]	gender considered in multiple logistic regression	male sex associated with wheezy bronchitis
Sherman et al., 1990 [52]	gender considered in various analyses	male sex associated with asthma; parental asthma and atopy increased risk of asthma in females not males; history of pneumonia, bronchitis, hay fever, or sinusitis exhibited no gender difference as risk factor for asthma

Table 9 shows that 36 of the 38 pulmonary function endpoint studies considered gender. In the majority of these, pulmonary function was, at least in certain analyses, adjusted for sex. One study observed no association for gender [65] and 2 studies were matched for gender [68, 72]. Of 11 studies that compared pulmonary function on the basis of gender, eight reported higher levels of some parameters in males [55, 58, 60, 61, 26, 66, 32, 74], two studies reported higher levels of certain parameters in females [64, 66] and one study, although reporting that gender affected pulmonary performance, provided little specific information [73].

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Table 9. Consideration of Gender of the Subject in Studies of Parental Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameter
Leeder et al., 1976 [55]	adjusted for gender	peak expiratory flow rates : boys > girls by multiple logistic regression
Schilling et al., 1977 [11]	gender	association between family history of asthma and pulmonary function affected by gender (i.e., particular functional parameters involved); maternal smoking associated with decreased $MEF_{50\%}$ (not FEV_1, PEFR) in girls, no association in boys
Yarnell/St. Leger, 1979 [56]	gender	maternal smoking associated with decrease in FMF and $FEV_{0.75}$ in girls not boys
Tager et al., 1976 [57]	adjusted for gender	association between maternal smoking and decreased FEV_1 in boys but not girls; parent-child correlations for FEV_1 for girls not boys
Tager et al., 1979 [15]	adjusted for gender	none reported
Weiss et al., 1980 [17]	adjusted for gender	none reported
Tager et al, 1983 [58]	adjusted for gender; gender considered in autoregressive model	male gender has positive influence on change in FEV_1 over a one year period
Tager et al., 1985 [59]	adjusted for gender; gender considered in autoregressive model	decrement in FEV_1 associated with smoking in males > females
O'Connor et al., 1987 [39]	adjusted for gender	none reported
Ware et al., 1984 [28]	adjusted for gender	none reported; no observed influence on maternal smoking association with pulmonary function
Berkey et al., 1986 [60]	adjusted for gender	unadjusted FEV_1 and FVC of boys > girls between 6-10 yrs of age
Hasselbad et al., 1981 [61]	gender	
Ekwo et al., 1983 [21]	gender	
Lebowitz et al., 1982 [62]	adjusted f	
Lebowitz, 1984 [25]	adjusted f	
Lebowitz et al., 1984 [63]	adjusted f	
Lebowitz et al., 1987 [64]	gender	
Lebowitz/Holberg, 198[illegible] [65]	gender	
Tashkin et al., 1984 [26]	gender	
Vedal et al., 1984 [66]	adjusted	

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ct in Studies of Parental
ction in Older Children

	Association of Parameter(s)
	peak expiratory flow rates of boys > girls by multiple logistic regression
	association between family history of asthma and pulmonary function affected by gender (i.e., particular functional parameters involved); maternal smoking associated with decreased $MEF_{50\%}$ (not FEV_1, PEFR) in girls, no association in boys
	maternal smoking associated with decrease in FMF and $FEV_{0.75}$ in girls not boys
	association between maternal smoking and decreased FEV_1 in boys but not girls; parent-child correlations for FEV_1 for rls not boys
	none reported
	none reported
	male gender has positive influence on change in FEV_1 over a one year period
	decrement in FEV_1 associated with smoking in males > females
	none reported
	none reported, no observed influence on maternal smoking association with pulmonary function
	unadjusted FEV_1 and FVC of boys > girls between ages yrs of age

Published Study	Parameter (ages)	Association of Parameter(s)
Hasselbad et al., 1981 [61]	gender	$FEV_{0.75}$ of boys > girls 6-13 yrs of age; maternal smoking associated with greater decrements in $FEV_{0.75}$ in boys than in girls; gas stove usage was associated with decreased $FEV_{0.75}$ in girls not in boys
Ekwo et al., 1983 [21]	gender	none reported
Lebowitz et al., 1982 [62]	adjusted for gender	none reported
Lebowitz, 1984 [25]	adjusted for gender	none reported
Lebowitz et al., 1984 [63]	adjusted for gender	none reported
Lebowitz et al., 1987 [64]	gender	$Vmax_{50}$/FVC of females aged 13-25 > males of the same age; gender was a significant co-variable in multivariate analysis of factors determining the relationship between symptoms, smoking and pulmonary function of children but not in relationship between asthma and pulmonary function (FEV_1 and $Vmax_{50}$)
Lebowitz/Holberg, 1987 [65]	gender	none observed for FEV_1, $Vmax_{50}$, and $Vmax_{50}$/FVC
Tashkin et al., 1984 [26]	gender	FVC, FEV_1, FEF_{25-75}, Vmax of males > females; age-gender influences on the association between maternal smoking and pulmonary function (ses Table 10)
Vedal et al., 1984 [66]	adjusted for gender	gender significant predictor of all pulmonary function parameters (FVC and $FEV_{0.75}$ boys > girls; FEF_{25-75}, $Vmax_{75}$, $Vmax_{50}$ girls > boys); significant interaction between gender and age for all functional parameters except FVC; maternal smoking associated with decreased flow rates in girls, no association with maternal smoking in boys

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Published Study	Parameter (ages)	Association of Parameter
Spinaci et al., 1985 [31]	gender	gender influenced association between geographic area (outdoor pollution) and pulmonary function, no gender influences observed with regard to associations between passive or active smoking and pulmonary function
Burchfiel et al., 1986 [32]	gender	age adjusted FEV_1 and FVC (males > females between [illegible] yrs of age; no consistent gender difference in $Vmax_{50}$; parental smoking decreased FEV_1 and FVC in males and $Vmax_{50}$ in females
Chen/Li, 1986 [67]	gender	paternal smoking was associated with greater decrements in FEV_1, MMEF and $FEF_{62.5-87.5}$ in girls than boys
Murray/Morrison, 1986 [68]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender	NA (matched)
Teculescu et al., 1986 [37]	exposed and nonexposed subjects matched for gender	parental smoking associated with decreased FEV_1 and FEF_{25-75} (not FVC or FEV_1/FVC) in boys not girls
Evans et al., 1987 [69]	gender	none reported
Stern et al., 1987, 1989 [40, 41]	adjusted for gender	none reported
Tsimoyianis et al., 1987 [42]	gender	association between ETS exposure and abnormal FEF_{25-75} or cough statistically significant in girls but not boys
Dijkstra et al., 1988 [44]	gender	NO_2 or gas stove usage was associated with decrements of pulmonary function growth in girls (FEV_1 and MMEF) not boys while household smoking was associated with decrements in pulmonary function growth in boys (PEF) not girls

Published Study	Parameter
Martinez et al., 1988 [70]	gender
Masi et al., 1988 [71]	gender
Murray/Morrison, 1988 [72]	exposed matic c for ma tion ac
Chan et al., 1989 [73]	adjuste
Kauffmann et al., 1989 [74]	gende

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Association of Parameter(s)
gender influenced association between geographic area (outdoor pollution) and pulmonary function; no gender influences observed with regard to association between passive or active smoking and pulmonary function
age adjusted FEV_1 and FVC of males > females between 10-19 yrs of age; no consistent gender difference in $Vmax_{50}$; parental smoking decreased FEV_1 and FVC in males and $Vmax_{50}$ in females
paternal smoking was associated with greater decrements in FEV_1, MMEF, and $FEF_{62.5-87.5}$ in girls than boys
asth- NA (matched)
parental smoking associated with decreased FEV_1 and FEF_{25-75} (not FVC or FEV_1/FVC) in boys not gurls
none reported
none reported
association between ETS exposure and abnormal FEF_{25-75} or cough statistically significant in girls but not boys
NO_2 or gas stove usage was associated with decrements in pulmonary function growth in girls (FEV_1 and MMEF not boys) while household smoking was associated with decrements in pulmonary function growth in boys (PEF) not girls

Published Study	Parameter (ages)	Association of Parameter(s)
Martinez et al., 1988 [70]	gender	parental smoking associated with increased bronchial responsiveness (carbachol) in males not females; amount of parental smoking associated with skin test reactivity in males not females; interaction between gender, parental smoking and atopy confirmed by multivariate analysis.
Masi et al., 1988 [71]	gender	duration of ETS exposure at home (persons X years) associated with decreased FEF_{25-75} and $Vmax_{50}$ (not FVC, FEV_1, PEFR) in males not females; ETS exposure in men (not women) before 17 years if age associated with decreased FEF_{25-75}
Murray/Morrison, 1988 [72]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender	NA (matched)
Chan et al., 1989 [73]	adjusted for gender	gender was a significant predictor of FVC, $FEV_{0.75}$, $MEF_{0.75}$, and PEFR; low birth weight was associated with a greater decrement of $FEV_{0.75}$ in boys than girls
Kauffmann et al., 1989 [74]	gender	FVC and FEV_1 boys > girls, no gender difference for FEF_{25-75}, FEV/FVC, or FEF_{25-75}/FVC; differences noted in brother-brother and sister-sister correlations of specific pulmonary function parameters; for most pulmonary function parameter correlations, like-sex sibships > opposite-sex sibships; gender differences in pulmonary function growth patterns observed; gender differences in parent-child correlations of specific pulmonary function parameters observed.

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Published Study	Parameter (ages)	Association of Parameter
Murray/Morrison, 1989 [75]	exposed and nonexposed asthmatic children comparable for male:female ratio; function adjusted for gender in some but not all analyses	maternal smoking associated with decreased FEV, FEF and PC_{20} (not FVC) in girls
Strachan et al., 1990 [53]	adjusted for gender	none reported

Eleven pulmonary function endpoint studies suggested an interaction between gender of the subject and parental/household smoking [11, 56, 57, 32, 67, 37, 42, 44, 70, 75]. An interaction between gender, age and parental household smoking was suggested in two studies [26, 71], and that of atopy and parental/household smoking in one study [70]. Although a significant number of studies reported the involvement of gender in the association between parental/household smoking and pulmonary function, there was no consistency of this association with males versus females. Interactions between gender of the subject and other variables were also suggested, including age [66], smoking [59], smoking and symptoms [64], indoor pollution [61, 44], outdoor pollution [31], family history of asthma [11], low birth weight [73], parent-child pulmonary function correlations [57, 74], and sibling-sibling pulmonary function correlations [74]. Eleven studies provided no information concerning any association between gender and pulmonary function [15, 17, 39, 28, 21, 62, 25, 63, 69, 40, 41, 53].

F. Active smoking by the subject

As shown in Table 10, 20 clinical endpoint studies considered active smoking as a potential confounder. The criteria employed to evaluate this factor varied significantly from study to study. In some, the data on active smoking were obtained from parental responses, while in others they were based on childhood responses in the absence of parents. Several studies assumed children to be nonsmokers below a certain age, although the cut-off age selected by particular studies ranged from 12 to 16 years. There was also variation in the criteria employed (e.g. number of cigarettes smoked, etc.) to classify a child as a smoker. Smokers were excluded or considered by the authors to be insignificant in nine of these studies [8, 10, 19, 26, 28, 37, 38, 42, 44]. Three studies reported no observed association between active smoking and respiratory conditions in children [17, 23, 52]. Four studies reported that active smoking was associated with increased prevalence of respiratory symptoms and disease in children [13, 24, 31, 54] and none reported an opposite association. Four studies provided no information with regard to any association between smoking and clinical endpoints [11, 32, 39, 51].

Table 10. Consideration of Active Sm
Household Smoking and R
Children

Published Study	Parameter
Cameron et al., 1969 [8]	2% of 13-1 smoking, in analysis
Lebowitz/Burrows, 1976 [10]	children sumed to 2 of 60 1- any smok smoked
Schilling et al., 1977 [11]	smoking from chil
Bland et al., 1978 [13]	all childr (groupec cigarette
Weiss et al., 1980 [17]	childhoc obtained respons parents
Dodge, 1982 [19]	children reporte
Schenker et al., 1983 [23]	whethe more c rently s respon
Charlton, 1984 [24]	quantit smoke
Tashkin et al., 1984 [26]	childre to be r asked and, if analys
Ware et al., 1984 [28]	childr higher status (1st t rental of sm fore r factor
Spinaci et al., 1985 [31]	childr one c smok

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Table 10. Consideration of Active Smoking by the Subject in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

Published Study	Parameter	Association of Parameter(s)
Cameron et al., 1969 [8]	2% of 13-16 yr olds reported smoking, apparently included in analysis	NA (homogeneous)
Lebowitz/Burrows, 1976 [10]	children under 15 were presumed to be nonsmokers (only 2 of 60 14 yr olds indicated any smoking and they had smoked very few cigarettes)	NA (homogeneous)
Schilling et al., 1977 [11]	smoking status obtained from child responses	none reported
Bland et al., 1978 [13]	all children questioned (grouped on basis of number cigarettes smoked)	associated with increased cough and breathlessness
Weiss et al., 1980 [17]	childhood smoking status obtained from subject's response in absence of parents	none observed for persistent wheeze
Dodge, 1982 [19]	children questioned, none reported smoking	NA (homogeneous)
Schenker et al., 1983 [23]	whether child smoked 5 or more cigarettes and is currently smoking (child's response)	none observed for respiratory symptoms (cough, phlegm, wheeze)
Charlton, 1984 [24]	quantity of cigarettes smoked/week (child response)	associated with increased cough
Tashkin et al., 1984 [26]	children under 12 assumed to be nonsmokers; others asked about smoking status and, if so, excluded from analysis	NA (homogeneous)
Ware et al., 1984 [28]	children in 4th grade or higher asked about smoking status in absence of parent (1st to 3rd grades from parental responses); incidence of smoking rare and, therefore not considered a risk factor	NA (homogeneous)
Spinaci et al, 1985 [31]	children who smoked at least one cigarette considered smokers (child's response)	associated with increased chronic cough

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Published Study	Parameter (ages)	Association of Parameter
Burchfiel et al., 1986 [32]	Children under 16 yrs. considered to be nonsmokers (active smoking by older children determined by questionnaire)	none reported
Teculescu et al., 1986 [37]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Willat, 1986 [38]	none of the children smoked (based upon parental responses)	NA (homogeneous)
O'Connor et al., 1987 [39]	obtained from child's responses; adjusted for in analysis	none reported
Tsimoyianis et al., 1987 [42]	smokers or ex-smokers were excluded from study (based upon subject's responses)	NA (homogeneous)
Dijkstra et al., 1988 [44]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Charlton/Blair, 1989 [54]	sometimes or regular smoking compared to no smoking (child response)	associated with increased school absence for a variety respiratory and nonrespiratory ailments
Neuspeil et al., 1989 [51]	from parental interview	none reported
Sherman et al., 1990 [52]	smoking status obtained from child's responses	none observed for asthma

27 pulmonary function endpoint studies considered active smoking by the subject as a potential confounding variable (Table 11). As in the clinical endpoint studies, there was significant variation as to whether this information was provided by parent or child, the age below which children were assumed to be nonsmokers (9-16 years), and the amount a child needed to smoke to be classified as a smoker. Children were excluded on the basis of active smoking or were considered to be of insignificant number in 14 studies [28, 60, 19, 26, 66, 67, 68, 37, 69, 42, 44, 71, 72, 75]. Six studies reported that active smoking was associated with decreased pulmonary function [15, 58, 59, 64, 65, 31], none reported an opposite association, and two studies reported no observed association between active smoking and pulmonary function [57, 17]. In five pulmonary function endpoint studies, no information was provided on this issue [11, 39, 62, 63, 32].

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Table 11: Consideration of Active Household Smoking an

Published Study	Parame
Schilling et al., 1977 [11]	smokir child re cluded
Tager et al., 1976 [57]	childh (detail althou parent old or
Tager et al., 1979 [15]	child's (obtai respo
Weiss et al., 1980 [17]	childr obtain in abs
Tager et al. 1983 [58]	child (obta respc
Tager et al., 1985 [59]	child (obta respc
O'Connor et al., 1987 [39]	obta pons anal
Ware et al., 1984 [28]	chilc high stat (1st pare of s ther risk
Berkey et al., 1986 [60]	chil at l wer (ea gra sm
Dodge, 1982 [19]	chi rep
Lebowitz et al., 1982 [62]	act sp

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...ssociation of Parameter(s)
...one reported
NA (homogeneous)
NA (homogeneous)
none reported
NA (homogeneous)
NA (homogeneous)
associated with increased school absence for a variety ...piratory and nonrespiratory ...ents
none reported
none observed for asthma

...dered active smoking by the ...1). As in the clinical endpoint ...hether this information was ... children were assumed to be ...ild needed to smoke to be ...on the basis of active smoking ...r in 14 studies [28, 60, 19, 2... ... reported that active smoking ...on [15, 58, 59, 64, 65, 31], none ...udies reported no observed ...nary function [57, 17]. In five ...tion was provided on this issue

Table 11. Consideration of Active Smoking by the Subject in Studies of Parental/Household Smoking and Pulmonary Function in Older Children

Published Study	Parameter	Association of Parameter(s)
Schilling et al., 1977 [11]	smoking status obtained from child responses; smokers excluded from analysis	none reported
Tager et al., 1976 [57]	childhood smoking history (details not specified although data obtained from parents for children 12 years old or less)	none observed for FEV_1 for males and females analyzed separately (stated that n was small)
Tager et al., 1979 [15]	child's smoking history (obtained from subject's responses)	associated with decreased FEF_{25-75}
Weiss et al., 1980 [17]	childhood smoking status obtained from subject's response in absence of parents	none observed for FEF_{25-75}
Tager et al, 1983 [58]	child's smoking history (obtained from subject's responses)	associated with decreased FEV_1 growth; effect on FEF_{25-75} borderline ($p=0.058$)
Tager et al., 1985 [59]	child's smoking history (obtained from subject's responses)	associated with decreased FEV_1 and FEF_{25-75}
O'Connor et al., 1987 [39]	obtained from child's responses; adjusted for in the analysis	none reported
Ware et al., 1984 [28]	children in 4th grade or higher asked about smoking status in absence of parent (1st to 3rd grades from parental responses; incidence of smoking rare and, therefore, not considered a risk factor	NA (homogeneous)
Berkey et al., 1986 [60]	children who currently smoked at least 1 cigarette/week were excluded from study (each child in 4th or higher grades asked about personal smoking habits)	NA (homogeneous)
Dodge, 1982 [19]	children questioned, none reported smoking	NA (homogenous)
Lebowitz et al., 1982 [62]	active smoking (details not specified)	none reported

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Published Study	Parameter	Association of Parameters
Lebowitz et al., 1984 [63]	based upon questionnaires completed by children 15 yr and older	none reported
Lebowitz et al., 1987 [64]	current, ex-, or never smoker (obtained from children 15 yrs or older, otherwise from parent)	current and ex-smoking associated with decreased FEV_1 and $Vmax_{xx}$ levels and growth rates, and $Vmax_{xx}$ F.
Lebowitz/Holberg, 1987 [65]	childhood smoking (details not specified)	active smoking asssociated with decreased $Vmax_{50}$ and $Vmax_{50\%}$/FVC, and FEV
Tashkin et al., 1984 [26]	children under 12 assumed to be nonsmokers; others asked about smoking status and, if so, excluded from analysis	NA (homogeneous)
Vedal et al., 1984 [66]	children considered smoker they smoked 5 or more cigarettes and were currently smoking (obtained from subject's responses in grades 4-6, not 1-3); smokers excluded from study	NA (homogeneous)
Spinaci et al., 1985 [31]	children who smoked at least one cigarette was considered a smoker (child's response)	active smoking associated with decreased $FEF_{25-75\%}$ and $Vmax_{50\%}$
Burchfiel et al., 1986 [32]	children under 16 yrs. considered to be nonsmokers (active smoking by older children determined by questionaire)	none reported
Chen/Li, 1986 [67]	children who reported smoking 1 or more cigarettes/wk. were rare and were excluded from the study (based on subject's responses)	NA (homogeneous)
Murray/Morrison, 1986 [68]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)
Teculescu et al., 1986 [37]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Evans et al., 1987 [69]	ever smoking children were excluded from study (subject's) responses)	NA (homogeneous)

Published Study	I
Tsimoyianis et al., 1987 [42]	
Dijkstra et al., 1988 [44]	
Masi et al., 1988 [71]	
Murray/Morrison, 1988 [72]	
Murray/Morrison, 1989 [75]	

G. Infant feeding

As shown in Table 12A, (i.e., presence or absence c milk) observed no associat between lack of breast fee provided no information or there were no pulmonary f dealt with infant feeding.

Table 12. Consideration of Household Smok Children

A. Infant feeding
Published Study
Fergusson/Horwood, 1985 [29]
Horwood et al., 1985 [30]
McConnochie/Roghmann, 1986 [33]
Willat, 1986 [38]

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Published Study	Parameter	Association of Parameter(s)
Tsimoyianis et al., 1987 [42]	smokers or ex-smokers were excluded from study (based upon subject's responses)	NA (homogeneous)
Dijkstra et al., 1988 [44]	smoking children excluded from study (based upon parental responses)	NA (homogeneous)
Masi et al., 1988 [71]	all nonsmokers based upon subject's questionnaire responses	NA (homogeneous)
Murray/Morrison, 1988 [72]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)
Murray/Morrison, 1989 [75]	active smokers omitted from study (obtained by subject's responses)	NA (homogeneous)

G. Infant feeding

As shown in Table 12A, three of the six studies that addressed infant feeding (i.e., presence or absence of breast feeding or comparison of breast, formula or milk) observed no association [30, 38, 51], one paper reported an association between lack of breast feeding and increased wheezing [33], and two papers provided no information on this issue [29, 43]. As indicated in Tables 1 and 13A, there were no pulmonary function endpoint studies in school-age children that dealt with infant feeding.

Table 12. Consideration of Selected Potential Confounders in Studies of Parental/Household Smoking and Respiratory Symptoms and Disease in Older Children

A. Infant feeding		
Published Study	Parameter	Association of Parameter(s)
Fergusson/Horwood, 1985 [29]	presence or absence of breast feeding	none reported
Horwood et al., 1985 [30]	early feeding history (breast and /or bottle) up to 4 mos of age	none observed for asthma
McConnochie/Roghmann, 1986 [33]	breast, formula, milk feeding during first 6 mos of life	lack of breast feeding assoc. with incr. wheezing (strongest among children without family history of allergy)
Willat, 1986 [38]	method of postnatal feeding	none observed for sore throats

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Published Study	Parameter	Association of Parameters
Andrae et al., 1988 [43]	type of feeding during first 6 mos.of life	none reported
Neuspeil et al., 1989 [51]	breast feeding at least 1 month	none observed for wheez, bronchitis
B. Outdoor pollution		
Published Study	Parameter	Association of Parameters
Kasuga et al., 1979 [14]	living distance from main highway as surrogate for amounts of NO_2 and SO_2 (<50 m, <100 m, >100 m); distance from highway based upon previous measurements of these gases	none observed for this parameter alone; however increased prevalence rate of respiratory diseases in children of heavy smoking households living <50 m of highway,suggestive of interaction between outdoor pollution and ETS exposure
Tager et al., 1979 [15]	outdoor air quality reported to be similar in various parts of the community	NA[1] (homogeneous)
Speizer et al., 1980 [16]	NO_2 monitoring outdoors in selected households	none reported
Dodge, 1982 [19]	towns with copper smelters vs. towns without copper smelters	none observed for asthma, wheeze, and sputum; increased prevalence of cough associated with towns with copper smelters.
Schenker et al., 1983 [23]	regions of low, medium, and high air pollution (based upon mining and power plants)	none reported
Charlton, 1984 [24]	industrial vs. non-industrial regions	none observed for prevalence of cough
Lebowitz, 1984 [25]	"random cluster sample" for TSPs, RSPs, CO, O_3, pollen, bacilli, fungi, and algae, over a 72 hr period	none reported
Ware et al., 1984 [28]	air quality variations among the 6 locations in this study were adjusted for by city-cohort correction in multiple logistic regression model	none reported

Published Study	Pa
Spinaci et al., 1985 [31]	ou by ar gr (t sa
Teculescu et al.,1986 [37]	st a p
Stern et al., 1987, 1989 [40, 41]	a w c
Andrae et al., 1988 [43]	c p f
Angioni et al., 1989 [47]	i s
C. Day care	
Published Study	
Said et al., 1978 [12]	
Willat, 1986 [38]	
Andrae et al., 1988 [43]	
McConnochie/Roghmann, 1089 [50]	
D. Animal exposures	
Published Study	
Fergusson/Horwood, 1985 [29]	
Horwood et al., 1985 [30]	
McConnochie/Roghmann, 1986 [33]	
Andrae et al., 1988 [43]	

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	Association of Parameter(s)
	none reported
n	none observed for wheezy bronchitis
	Association of Parameter(s)
	none observed for this parameter alone; however, increased prevalence rate of respiratory diseases in children of heavy smoking households living <50 m of highway suggestive of interaction between outdoor pollution and ETS exposure
	NA[1] (homogeneous)
of	
	none reported
	ıe observed for asthma, .heeze, and sputum; increased prevalence of cough associated with towns with copper smelters
d	none reported
s)	
	none observed for prevalence of cough
	none reported
	none reported
e	

Published Study	Parameter	Association of Parameter(s)
Spinaci et al., 1985 [31]	outdoor pollution (monitored by daily measurement of SO_2 and TSPs) was basis of 3 geographic areas, central urban (UC), peripheral (UP), and suburban (SU).	bronchial secretions with colds increased (boys not girls) in UC and UP compared to SU; asthma increased (boys not girls) in SU compared to UC and UP; none observed for cough, wheeze, shortness of breath, infant or recent respiratory illness.
Teculescu et al.,1986 [37]	subjects recruited from an area without significant air pollution	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all towns examined were small with no significant sources of industrial air pollution	NA (homogeneous)
Andrae et al., 1988 [43]	compared area near pulp and paper plant to area farthest from plant	associated with increased bronchial hyperreactivity and allergic disease
Angioni et al., 1989 [47]	industries, workshops, jointers shops, bakeries near house	none observed for allergic respiratory and nonrespiratory disease
C. Day care		
Published Study	Parameter	Association of Parameter(s)
Said et al., 1978 [12]	day care before age of 3	day care associated with increased incidence of adenoidectomy and/or tonsillectomy
Willat, 1986 [38]	age starting at day care or nursery	none reported
Andrae et al., 1988 [43]	type of daily care for pre-schoolers	none reported
McConnochie/Roghmann, 1089 [50]	"pre-school experience"	none observed for wheezing or asthma
D. Animal exposures		
Published Study	Parameter	Association of Parameter(s)
Fergusson/Horwood, 1985 [29]	duration of household pet ownership	none reported
Horwood et al., 1985 [30]	ownership of pet cat or dog	none observed
McConnochie/Roghmann, 1986 [33]	pets in home	none observed
Andrae et al., 1988 [43]	caged birds, aquarium fish, and furred pets in home	none observed

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Published Study	Parameter	Association of Parameter(s)
Dijkstra et al., 1988 [44]	animals at home	none reported
Angioni et al., 1989 [47]	pets in house	none observed
Chan et al., 1989 [49]	pets in house	none reported
McConnochie/Roghmann, 1989 [50]	dog or cat present in home	none observed
E. Stress		
Published Study	Parameter	Association of Parameter(s)
Fergusson/Horwood, 1985 [29]	quantitative score for stressful events in mother's life	none reported
Horwood et al., 1985 [30]	quantitative scores for stressful events inmother's life and maternal depression	none observed
Neuspeil et al., 1989 [51]	quantitative score of maternal depression	none reported
[1]Not applicable		

Table 13. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Pulmonary Function in Older Children

A. Infant feeding - no studies		
B. Outdoor pollution		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	outdoor air quality reported to be similar in various parts of the community	NA (homogeneous)
Speizer et al., 1980 [16]	NO_2 monitoring outdoors in selected households	none reported
Ware et al., 1984 [28]	air quality variations among the 6 locations in this study were adjusted for by city-cohort correction in multiple logistic correction model	none reported
Hasselblad et al., 1981 [61]	ambient air pollution measurement of TSPs, RSPs, and water soluble sulfate fraction of TSPs	none observed for $FEV_{0.75}$
Dodge, 1982 [19]	towns with copper smelters vs. towns without copper smelters	none observed for FEV_1

Published Study	Paramet
Lebowitz et al., 1982 [62]	measure outdoor household low; par and NC in exce
Lebowitz, 1984 [25]	"randor TSPs, F bacilli. over a
Tashkin et al., 1984 [26]	adjustu area
Spinaci et al., 1985 [31]	outdo by da and T graph (UC). subur
Chen/Li, 1986 [67]	outdc cons: subje samp
Teculescu et al., 1986 [37]	subje with
Stern et al., 1987, 1989 [40, 41]	all t with of ir
Kauffmann et al., 1989 [74]	tow
C. Day care - no studies	

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Association of Parameter(s)
none reported
none observed
none reported
none observed

Association of Parameter(s)
none reported
none observed
none reported

anders in Studies of Parental
action in Older Children

	Association of Parameter(s)
to	NA (homogeneous)
	none reported
	none reported
e	
ure- ater TSPs	none observed for FEV
s vs lters	none observed for FEV

Published Study	Parameter	Association of Parameter(s)
Lebowitz et al., 1982 [62]	measurement of a variety of outdoor pollutants in selected households (CO was considered low; particulatesconsidered high; and NO2 was variable but not in excess of NAAQS).	NA (homogeneous)
Lebowitz, 1984 [25]	"random cluster sample" for TSPs, RSPs, CO, O_3, pollen, bacilli, fungi, and algae over a 72 hr period	children's Vmax inversely associated with TSPs and O_3 as an interaction; O_3 associated with Vmax in children not exposed to ETS.
Tashkin et al., 1984 [26]	adjustment for geographical area	none reported
Spinaci et al., 1985 [31]	outdoor pollution (monitored by daily measurement of SO_2 and TSPs) was basis of 3 geographic areas, central urban (UC), peripheral (UP), and suburban (SU).	UC and UP associated with decreased FEV_1 and FVC
Chen/Li, 1986 [67]	outdoor urban air pollution considered the same for all subjects because area of sample collection small	NA (homogeneous)
Teculescu et al., 1986 [37]	subjects recruited from an area without significant air pollution	NA (homogeneous)
Stern et al., 1987, 1989 [40, 41]	all towns examined were small with no significant sources of industrial pollution	NA (homogeneous)
Kauffmann et al., 1989 [74]	town of residence	none reported
C. Day care - no studies		

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D. Animal exposures		
Published Study	Parameter	Association of Parameters
Murray/Morrison, 1986 [68]	matched for ownership of household pets	NA (matched)
Murray/Morrison, 1988 [72]	matched for ownership of furred household pets	none observed when tested by multiple regression on a seasonal basis
Chan et al., 1989 [73]	pets in house	none reported
Murray/Morrison, 1989 [75]	matched for ownership of dogs or cats and positive skin prick tests to appropriate species	NA (matched)
E. Stress		
Published Study	Parameter	Association of Parameter(s)
Evans et al., 1987 [69]	general stress in household	none reported

H. Outdoor pollution

As shown in Table 12B, the 13 clinical endpoint papers that considered outdoor pollution employed a variety of criteria for this particular potential confounder, including proximity to an area of pollution (e.g., highway or industrial source), residence within an industrial area, and measured levels of industrial pollution using specific environmental markers. Four of the studies reported no observed association [14, 24, 31, 47] and three reported positive associations between outdoor pollution and particular clinical endpoints [19, 31, 43]. One study suggested an interaction between outdoor pollution and parental/household smoking [14]. In three of these studies, the outdoor air quality of the area(s) was judged to be similar or homogeneous by the authors [15, 37, 40, 41], while four papers provided no information pertaining to associations [16, 23, 25, 28].

As shown in Table 13B, outdoor pollution (i.e., on the basis of proximity to industrial areas or environmental markers) was considered in 13 of these studies. Outdoor air quality was regarded as being homogeneous in five studies [15, 62, 67, 37, 40, 41]. No association with outdoor pollution was reported to be observed in two studies [61, 19], while a "negative" association between particular pulmonary function parameters and outdoor pollution was reported in two studies [25, 31]. Four studies reported no information on any association between outdoor pollution and pulmonary function endpoints [16, 28, 26, 74].

I. Day care

Of the four clinical endpoint studies that dealt with day care use as a potential confounder, one reported no observed association [50], one reported a "positive" association [12], and two provided no information relative to any association [38,

43] (Table 12 C). As indic
function endpoint studies c

J. Animal exposures

Five of the eight studies
cated furred pets) reported
33, 43, 47, 50] while the
information (Table 12 D). F
pets) as a potential confc
studies. Of these, two wer
observed association [72],
(Table 13 D).

H. Stress

The three clinical enc
confounder employed a q
as a confounding variable
and two provided no info:
general stress in the hou
endpoint study [69] in whi
13 E).

I. Dampness and cold

As shown in Table 14 A
and cold as a potential c
outdoor humidity; indoor
and/or dampness in the c
observed in two of the
dampness and cold in th
increased rates of respira
studies provided no infor
with clinical endpoints [.

Of the four pulmona
and cold (e.g., outdoor a
and cold/wet season vs.
ent association but an as
maternal smoking and as
44, 73] (Table 15A).

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	Association of Parameter(s)
	NA (matched)
	none observed when tested by multiple regression on a seasonal basis
	none reported
...gs ...ck	NA (matched)

	Association of Parameter(s)
...	none reported

...point papers that considered ...a for this particular potential ...f pollution (e.g., highway or ... and measured levels of ...ers. Four of the studies ...] and three reported positive ...cular clinical endpoints [19, 31, ...outdoor pollution and parental ...es, the outdoor air quality of the ...s by the authors [15, 37, 40, 41]. ...ining to associations [16, 23, 25, ...

...e., on the basis of proximity to ...considered in 13 of these studies ...ogeneous in five studies [15, 62 ... pollution was reported to be ...negative" association between ...outdoor pollution was reported ...o information on any association ...action endpoints [16, 28, 2...

...lt with day care use as a potential ...ion [50], one reported a "positive ...on relative to any associati...

43] (Table 12 C). As indicated in Tables 1 and 13C, none of the pulmonary function endpoint studies dealt with day care.

J. Animal exposures

Five of the eight studies that dealt with animal exposures (mainly domesticated furred pets) reported no observed association with a clinical endpoint [30, 33, 43, 47, 50] while the remaining three [29, 44, 49] provided no relevant information (Table 12 D). Four studies considered animal exposures (household pets) as a potential confounding variable in pulmonary function endpoints studies. Of these, two were considered to be matched [68, 75], one reported no observed association [72], and one provided no information on the issue [73] (Table 13 D).

H. Stress

The three clinical endpoint papers that considered stress as a potential confounder employed a quantitative score of maternal stress and/or depression as a confounding variable. One of these reported no observed association [30] and two provided no information on this issue [29, 51] (Table 12 E). Stress (i.e., general stress in the household) was considered in one pulmonary function endpoint study [69] in which no information on associations was provided (Table 13 E).

I. Dampness and cold

As shown in Table 14 A, seven clinical endpoint studies considered dampness and cold as a potential confounder based upon the following types of criteria: outdoor humidity; indoor humidity; domestic dampness and mold; and coldness and/or dampness in the child's bedroom or home. No association was reported observed in two of the studies [47, 49], while three studies, all involving dampness and cold in the child's bedroom or home, reported associations with increased rates of respiratory symptoms and disease in subjects [36, 43, 50]. Two studies provided no information concerning dampness and cold and associations with clinical endpoints [25, 44].

Of the four pulmonary function endpoint studies that considered dampness and cold (e.g., outdoor and indoor humidity, dampness and/or cold in the home and cold/wet season vs. warm/dry season), one reported no observed independent association but an association suggestive of an interaction between season, maternal smoking and asthma [72], while three provided no such information [25, 44, 73] (Table 15A).

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Table 14. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Respiratory Symptoms and Disease in Older Children

A. Dampness and cold		
Published Study	Parameter	Association of Parameter(s)
Lebowitz, 1984 [25]	outdoor and indoor humidity	none reported
Strachan/Elton, 1986 [36]	dampness/mold in home; bedroom environment (cold)	dampness/mold associated with increased rates of wheezing, school absences due to lower respiratory problems, and coughing; bedroom environment associated with increased wheezing.
Andrae et al., 1988 [43]	signs of damage due to dampness in home	associated with increased coughing after respiratory infections (not asthma, allergic rhinitis, or exercise-induced cough).
Dijkstra et al., 1988 [44]	dampness in the house	none reported
Angioni et al., 1989 [47]	absence of heating in home	none observed
Chan et al., 1989 [49]	dampness or cold in home	none observed
Neuspeil et al., 1989 [50]	dampness in child's bedroom	associated with increased wheezy bronchitis
B. Heating and air conditioning		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	homes with central gas heating vs. other	none reported
Speizer et al., 1980 [16]	home heating fuel (oil, gas, electric); presence or absence of air conditioning	none observed
Weiss et al, 1980 [17]	gas heater in kitchen heating	none observed
Ware et al., 1984 [28]	fuel and air conditioning (dropped from regression)	none reported
Spinaci et al., 1985 [31]	presence or absence of central heating	none reported
McConnochie/Rohgmann 1986 [33]	home heating method	none observed
Strachan/Elton, 1986 [36]	type of heat (gas or coal)	coal burning associated with increased coughing
Andrae et al., 1988 [43]	type of heating	none reported
Angioni et al., 1989 [47]	type of heating (radiators, electric, gas, firewood, none)	none observed

Published Study	Parameter
Berwick et al., 1989 [48]	type of he from tax a
Chan et al., 1989 [49]	type of fu heating
McConnochie/Roghmann 1989 [50]	home hea
C. Season	
Published Study	Paramete:
Colley et al., 1974 [9]	cough in
Bland et al., 1978 [13]	study cor
Charlton, 1984 [24]	question istered d of Decen variation epidemic
Lebowitz, 1984 [25]	season
Park/Kim, 1986, 1988 [34, 35]	season
Strachan/Elton, 1986 [36]	conducte season
Tsimoyianis et al, 1987 [42]	conducte
Dijkstra et al., 1988 [44]	questior symptor
D. Occupational exposures - no studi	
E. Quality of housing	
Published Study	Paramet
Kasuga et al., 1979 [14]	structure reinforc
Park/Kim 1986, 1988 [34, 35]	number in a hou
Strachan/Elton, 1986 [36]	145 of 1 in local
Andrae et al., 1988 [43]	type of buildin carpetir
Berwick et al., 1989 [48]	from ta (assesse used, c numbe floors, bottom
Chan et al., 1989 [49]	home c

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inders in Studies of Parental/
ptoms and Disease in Older

	Association of Parameter(s)
	none reported
	dampness/mold associated with increased rates of wheezing, school absences due to lower respiratory problems, and coughing; bedroom environment associated with increased wheezing.
	associated with increased coughing after respiratory infections (not asthma, allergic rhinitis, or exercise-induced cough).
	none reported
	none observed
	none observed
	associated with increased wheezy bronchitis

	ociation of Parameter(s)
	none reported
	none observed
	none observed
	none reported
	none reported
	none observed
	coal burning associated with increased coughing
	none reported
	none observed

Published Study	Parameter	Association of Parameter(s)
Berwick et al., 1989 [48]	type of heating and fuel used from tax assessor's records	none reported
Chan et al., 1989 [49]	type of fuel used for home heating	none reported
McConnochie/Roghmann 1989 [50]	home heating method	none observed
C. Season		
Published Study	Parameter	Association of Parameter(s)
Colley et al., 1974 [9]	cough in winter as endpoint	NA (homogeneous)
Bland et al., 1978 [13]	study conducted in July	NA (homogeneous)
Charlton, 1984 [24]	questionnaires were administered during the first week of December to minimize variations due to local season epidemics	NA (homogeneous)
Lebowitz, 1984 [25]	season	none reported
Park/Kim, 1986, 1988 [34, 35]	season	none observed
Strachan/Elton, 1986 [36]	conducted during winter season	NA (homogeneous)
Tsimoyianis et al, 1987 [42]	conducted during August	NA (homogeneous)
Dijkstra et al., 1988 [44]	questions on respiratory symptoms gathered in winter	NA (homogeneous)
D. Occupational exposures - no studies		
E. Quality of housing		
Published Study	Parameter	Association of Parameter(s)
Kasuga et al., 1979 [14]	structure of house (wood vs. reinforced concrete)	none observed
Park/Kim 1986, 1988 [34, 35]	number of rooms occupied in a house	none observed
Strachan/Elton, 1986 [36]	145 of 165 children lived in local authority housing	NA (homogeneous)
Andrae et al., 1988 [43]	type of house (construction, building material, wall to wall carpeting)	none observed
Berwick et al., 1989 [48]	from tax assessor records (assessed value, materials used, condition of home, age, number of rooms, number of floors, square footage of bottom floor)	none observed
Chan et al., 1989 [49]	home condition	none reported

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J. Heating and air conditioning

Among the 12 clinical endpoint studies that considered heating and air conditioning, several criteria were employed, such as type of home heating fuel, presence or absence of air conditioning, and presence or absence of home heating (Table 14 B). Of these, five studies reported no observed association of this variable (usually pertaining to home heating) with clinical endpoints [16, 17, 33, 47, 50], while one study reported an association between coughing and the use of coal burning [36]. Six of these studies provided no information relative to any association with this particular potential confounding variable [15, 28, 31, 43, 48, 49].

Heating and air conditioning (i.e., type of home heating fuel, presence or absence of air conditioning, or presence or absence of central heating) were considered in nine pulmonary function endpoint studies (Table 15 B). Of these, one was considered to be homogeneous with regard to this potential confounder [62], three reported no observed association [16, 70, 72], and two reported that the type of home heating influenced pulmonary function [16, 31]. Four studies provided no information on the relationship between this potential confounder and pulmonary function [15, 28, 73, 75].

Table 15. Consideration of Selected Potential Confounders in Studies of Parental Household Smoking and Pulmonary Function in Older Children

A. Dampness and cold		
Published Study	Parameter	Association of Parameter(s)
Lebowitz, 1984 [25]	outdoor and indoor humidity	none reported
Dijkstra et al., 1988 [44]	dampness in the house	none reported
Murray/Morrison, 1988 [72]	cold/wet season vs. warm/dry season	none observed for for FEV_1, FEF_{25-75}, and PC_{20} to histamine in asthmatic children of nonsmoking mothers although decrements of above observed in asthmatic children of smoking mothers compared to children of non-smoking mothers during cold/wet season.
Chan et al., 1989 [73]	dampness or cold in home	none reported
B. Heating and air conditioning		
Published Study	Parameter	Association of Parameter(s)
Tager et al., 1979 [15]	homes with central gas heating vs. other	none reported

Published Study	Parame
Speizer et al., 1980 [16]	home h electric of air c
Ware et al., 1984 [28]	heatin from r
Lebowitz et al., 1982 [62]	most h heat a
Spinaci et al., 1985 [31]	prese: centra
Martinez et al., 1988 [70]	sourc (cent gas, c
Murray/Morrison, 1988 [72]	type of w
Chan et al., 1989 [73]	type heat
Murray/Morrison, 1989 [75]	use

C. Season	
Published Study	Para
Yarnell/St. Leger, 1979 [56]	all p perf mo
Ware et al., 1984 [28]	sea pul
Hasselblad et al., 1981 [61]	sea pul
Lebowitz, 1984 [25]	sea pe
Spinaci et al., 1985 [31]	stu wi Af
Chen/Li, 1986 [67]	stu
Tsimoyianis et al., 1987 [42]	st
Dijkstra et al., 1988 [44]	pu in
Martinez et al., 1988 [70]	p d N

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...nsidered heating and air
...type of home heating fuel,
...ence or absence of home
...no observed association of
...n clinical endpoints [16, 17,
...between coughing and the
...information relative to any
...riable [15, 28, 31, 43, 48, 49].
...heating fuel, presence or
...e of central heating) were
...lies (Table 15 B). Of these,
...o this potential confounder
...72], and two reported that
...ction [16, 31]. Four studies
...n this potential confounder

...nders in Studies of Parental
...ction in Older Children

...ciation of Parameter(s)
...reported
none reported
none observed for for FEV_1, FEF_{25-75}, and PC_{20} to histamine in asthmatic children of nonsmoking mothers although decrements of above observed in asthmatic children of smoking mothers compared to children of nonsmoking mothers during cold/wet season
none reported

Association of Parameter(s)
none reported

Published Study	Parameter	Association of Parameter(s)
Speizer et al., 1980 [16]	home heating fuel (oil, gas, electric); presence or absence of air conditioning	FEV_1 residuals vary as follows for home heating fuel: oil> gas>electric; none observed for presence or absence of air conditioning
Ware et al., 1984 [28]	heating fuel and air (dropped from regression)	none reported
Lebowitz et al., 1982 [62]	most homes had central heat and air conditioning	NA (homogeneous)
Spinaci et al., 1985 [31]	presence or absence of central heating	central heating associated with increased FVC
Martinez et al., 1988 [70]	source of energy for heating (centralized, kerosene, natural gas, other)	none observed for bronchial responsiveness
Murray/Morrison, 1988 [72]	type of central heating and use of wood stoves for heating	none observed for various types of home heating
Chan et al., 1989 [73]	type of fuel used for home heating	none reported
Murray/Morrison, 1989 [75]	use of wood stove for heating	none reported

C. Season

Published Study	Parameter	Association of Parameter(s)
Yarnell/St. Leger, 1979 [56]	all pulmonary function performed during summer months	NA (homogeneous)
Ware et al., 1984 [28]	seasonal adjustment for pulmonary function	none reported
Hasselblad et al., 1981 [61]	seasonal adjustment for pulmonary function	none reported
Lebowitz, 1984 [25]	seasonal adjustment for peak flow	none reported
Spinaci et al, 1985 [31]	study conducted during winter season (October to April)	NA (homogeneous)
Chen/Li, 1986 [67]	study conducted in June	NA (homogeneous)
Tsimoyianis et al., 1987 [42]	study conducted in August	NA (homogeneous)
Dijkstra et al., 1988 [44]	pulmonary function measured in spring and autumn	NA (homogeneous)
Martinez et al., 1988 [70]	pulmonary function measured during September and November	NA (homogeneous)

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Published Study	Parameter	Association of Parameter(s)
Murray/Morrison, 1988 [72]	cold, wet season (October through May) vs. warm, dry season (June through September)	none observed for FEV$_1$, FEF_{25-75}, and PC_{20} to histamine in asthmatic children of nonsmoking mothers, although decrements of above were observed in asthmatic childen of smoking mothers compared to children of nonsmoking mothers during the cold, wet season
D. Occupational exposures		
Published Study	Parameter	Association of Parameter(s)
Kauffmann et al. 1989 [74]	parents were chosen from white collar workers to decrease any possible influence of parental exposure to industrial pollutants	NA (homogeneous)
E. Quality of housing		
Published Study	Parameter	Association of Parameter(s)
Lebowitz et al., 1982 [62]	housing quality said to be relatively uniform	NA (homogeneous)
Chan et al., 1989 [73]	home condition	none reported

K. Seasons

As shown in Table 14 C, eight clinical endpoint studies considered season (i.e., time of year when questionnaire was administered or when endpoint was to have occurred). Of these studies, six were considered homogeneous with regard to season [9, 13, 24, 36, 42, 44], while one study reported no observed association [34, 35] and one study provided no information on this variable [25].

As shown in Table 15 C, the criteria for consideration of season pertained to when pulmonary measurements were taken. Of the 10 relevant studies, six were considered to be homogeneous [56, 31, 67, 42, 44, 70], one reported no independent association but a possible interaction of asthma, maternal smoking and season [72], while the remaining three studies provided no relevant data [28, 61, 25].

L. Occupational exposures

No clinical endpoint studies dealt with occupational exposures of the parent or child as a potential confounding variable (Table 1 and Table 14 D). As shown in Table 15 D, one study [74] employed only white collar worker families to minimize occupational exposures of the subjects and was, thus, judged to be homogenous with regard to occupational exposures.

M. Quality of housing

Several criteria were variat
considered quality of housing
were basic structure of the ho
home and particular aspects c
assessed value (Table 14 E).
association with a clinical end
be homogeneous [36] and on

Housing quality was cons
endpoint studies, with one j
provided no information on t

Our recent analysis of t
revealed that several factors
between household/parental
toms and diseases and pulm
or older children [7]. Firstly, t
wheeze, asthma, or bronchit
parents or adult household m
or medical records in only e
the 21 potential confounde
question. For example, onl
nomic status, age, gender, g
location of residence, and a
majority of the clinical anc
studies, while several of
dampness/cold, occupation
received little or no attention
of the potential confounders
study with regard to the par
that they were considered

In our previous report,
variables (i.e., socioeconon
health history, personal hea
to study in the criteria us
socioeconomic status, fami

The current report exter
the remaining 16 confounc
analysis reveals wide var

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sociation of Parameter(s)
ne observed for FEV_1, F_{25-75}, and PC_{20} to tamine in asthmatic ildren of nonsmoking others, although decrements above were observed in hmatic childen of smoking others compared to children nonsmoking mothers ring the cold, wet season.
ssociation of Parameter(s)
A (homogeneous)
ssociation of Parameter(s)
A (homogeneous)
c ported

adies considered season d or when endpoint was ered homogeneous with ly reported no observed tion on this variable [25]

n of season pertained to relevant studies, six were , 70], one reported no sthma, maternal smoking no relevant data [28, 61, 25]

l exposures of the parent d Table 14 D). As shown collar worker families was, thus, judged

M. Quality of housing

Several criteria were variably used in the six clinical endpoint studies that considered quality of housing as a potential confounding variable. Among these were basic structure of the home (wood vs. concrete), number of rooms in the home and particular aspects of the home, such as condition, square footage or assessed value (Table 14 E). Of these six studies, four reported no observed association with a clinical endpoint [14, 34, 35, 43, 48], while one was judged to be homogeneous [36] and one provided no relevant information [49].

Housing quality was considered as a variable in two pulmonary function endpoint studies, with one judged to be homogeneous [62] while the other provided no information on this issue [73] (Table 15 E).

DISCUSSION

Our recent analysis of the treatment of potential confounding variables revealed that several factors could explain the lack of consistent association between household/parental smoking and the prevalence of respiratory symptoms and diseases and pulmonary function endpoints in studies of school age or older children [7]. Firstly, the clinical endpoints (such as prevalence of cough, wheeze, asthma, or bronchitis) were based largely on subjective responses of parents or adult household members and were verified by physical examination or medical records in only eight of the 45 studies. Secondly, relatively few of the 21 potential confounders identified were considered in the studies in question. For example, only eight of the 21 potential confounders (socioeconomic status, age, gender, gas stove usage, personal health history, family size, location of residence, and active smoking by subject) were considered in the majority of the clinical and/or pulmonary function endpoint epidemiologic studies, while several of the confounders (infant feeding, day care use, dampness/cold, occupational exposures, quality of housing, nutritional status) received little or no attention. In addition, most studies considered relatively few of the potential confounders and there was considerable variation from study to study with regard to the particular confounders considered, as well as the way that they were considered (i.e., statistical testing).

In our previous report, detailed analysis of selected potential confounding variables (i.e., socioeconomic status, gas stove usage, indoor pollution, family health history, personal health history) revealed significant variation from study to study in the criteria used for each variable, particularly in the case of socioeconomic status, family health history, and personal health history [7].

The current report extends these initial observations by examining in detail the remaining 16 confounding variables from the list of 21 such factors. This analysis reveals wide variation in the criteria used for several particular

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confounders, most notably family size, location of residence, age of the subject, active smoking, outdoor pollution, dampness and cold, type of heating air conditioning, and quality of housing.

Since confounders alone or in combination could potentially influence the outcome of epidemiologic studies, despite their consideration and/or adjustment in such studies [6], examination of the consistency of association between such factors and endpoints would seem to be an important endeavor. An indication of whether or not there was a consistent association from study to study relative to a particular confounder can be obtained by consideration of only those studies that addressed such an association (i.e., after exclusion of studies where confounders were judged by the authors to be matched, homogenous, or where associations were not reported). A consistency of association or lack of association is based upon whether the majority of studies favor an increase, decrease, or no association between the variable in question and the endpoint. These data for both the previous and current analysis are summarized for clinical and pulmonary function endpoints in Tables 16 and 17, respectively.

Our previous analysis revealed that family health history and personal health history were consistently associated with an increased prevalence of respiratory symptoms and disease (Table 16), while personal health history was consistently associated with decreased pulmonary function (Table 17) in index children. No association was consistently observed between clinical endpoints and gas stove usage/indoor pollution (Table 16) or between pulmonary function endpoints and socioeconomic status or family health history (Table 17). The results were equivocal (no consistent trend) with regard to socioeconomic status and clinical endpoints (Table 16), as well as gas stove/indoor pollution and pulmonary function endpoints (Table 17) [7].

The current report extends these observations. The majority of studies pertaining to gender indicate that males are more at risk for respiratory symptoms and diseases (Table 16). Among the factors found to consistently influence pulmonary function in index children were gender, age, active smoking and location of residence (Table 17). No association was consistently observed for clinical endpoints and family size, heating/air conditioning, animal exposures, quality of housing, and infant feeding (Table 16) and for pulmonary function endpoints and family size (Table 17). Caution should be exercised with regard to interpretation of a consistent lack of association between a potential confounder and an endpoint. Although such consistency may indicate that such confounders have little influence on the outcome of the study, this lack of association could also be a reflection of the wide variation from study to study in the criteria used for such variables, the fact that clinical endpoints were, for the most part unverified, and, in some cases, the relatively small number of studies involved.

Table 16. Associations Betwe Endpoints

Increased/Decreased Prevalence of
Family health history (increa
Personal health history (incre
Gender (males increased, 13
No Association Observed
Gas stove use/indoor polluti
Family size (10 of 13 studies
Heating/air conditioning (5
Animal exposures (5 of 5 stu
Quality of housing (3 of 4 st
Infant feeding (3 of 4 studie
Equivocal/Uncertain Association c
Socioeconomic status (20 st
Location of residence (8 stu
Age (17 studies)
Active smoking (7 studies)
Outdoor pollution (6 studie
Dampness and cold (5 stud
Day care use (2 studies)
Season (1 study)
Stress (1 study)
Occupational exposures (0
Nutrition (0 studies)

[a]Number of studies after exclusion

In the current analysis th with regard to location o dampness/cold, day care, se pulmonary function endpoi animal exposures, dampness/ could be due either to variati of studies involved. Also, as in to study could reflect lack of or use of unverified subject

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ience, age of the subject,
old, type of heating/air

potentially influence the
eration and/or adjustment
association between such
endeavor. An indication
om study to study relative
ation of only those studies
lusion of studies where
d, homogenous, or where
f association or lack of
tudies favor an increase,
uestion and the endpoint.
re summarized for clinical
17, respectively.
istory and personal health
prevalence of respiratory
th history was consistently
17) in index children. No
al endpoints and gas stove
onary function endpoints
ah 7). The results were
c ic status and clinical
pollution and pulmonary

The majority of studies
sk for respiratory symptoms
d to consistently influence
, age, active smoking and
s consistently observed for
itioning, animal exposures
nd for pulmonary function
ld be exercised with regard
ation between a potential
ency may indicate that such
e of the study, this lack of
ariation from study to study
clinical endpoints were for
relatively small number of

Table 16. Associations Between Potential Confounding Variables and Clinical Endpoints

Increased/Decreased Prevalence of Symptoms/Diseases
Family health history (increased, 16 of 17 studies[a])
Personal health history (increased, 11 of 11 studies)
Gender (males increased, 13 of 23 studies)
No Association Observed
Gas stove use/indoor pollution (13 of 15 studies)
Family size (10 of 13 studies)
Heating/air conditioning (5 of 6 studies)
Animal exposures (5 of 5 studies)
Quality of housing (3 of 4 studies)
Infant feeding (3 of 4 studies)
Equivocal/Uncertain Association or No Data Available
Socioeconomic status (20 studies)
Location of residence (8 studies)
Age (17 studies)
Active smoking (7 studies)
Outdoor pollution (6 studies)
Dampness and cold (5 studies)
Day care use (2 studies)
Season (1 study)
Stress (1 study)
Occupational exposures (0 studies)
Nutrition (0 studies)
[a]Number of studies after exclusion of those matched, homogenous, and not reported

In the current analysis the associations are equivocal for clinical endpoints with regard to location of residence, active smoking, outdoor pollution, dampness/cold, day care, season, stress, and age of subject (Table 16) and for pulmonary function endpoints and heating/air conditioning, outdoor pollution, animal exposures, dampness/cold, and season (Table 17). Equivocal associations could be due either to variation of result from study to study, or the small number of studies involved. Also, as in the case of lack of association, variation from study to study could reflect lack of standardization of criteria for confounding variables or use of unverified subjective responses as clinical endpoints.

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Table 17. Associations Between Potential Confounding Variables and Pulmonary Functional Endpoints

Increased/Decreased Pulmonary Function
Personal health history (decreased, 12 of 15 studies*)
Age (increased, 11 of 12 studies)
Gender (males increased, 9 of 10 studies)
Active smoking (decreased, 6 of 8 studies)
Location of residence (decreased, 4 of 5 studies)
No Association Observed
Socioeconomic status (9 of 13 studies)
Family health history (7 of 8 studies)
Family size (7 of 7 studies)
Equivocal/Uncertain Association or No Data Available
Gas stove use/indoor pollution (11 studies)
Heating/air conditioning (4 studies)
Outdoor pollution (4 studies)
Animal exposures (1 study)
Dampness and cold (1 study)
Season (1 study)
Stress (0 studies)
Infant feeding (0 studies)
Nutrition (0 studies)
Quality of housing (0 studies)
Day care use (0 studies)
Occupational exposures (0 studies)
*Number of studies after exclusion of those matched, homogeneous, and not reported.

Taken together, the results of this analysis and the previous analyses of the published epidemiologic data in school-age children [1-3, 7] indicate lack of a consistent association between parental/household smoking and respiratory clinical and pulmonary function endpoints in these children, inconsistent and inadequate treatment of potential confounding variables and inadequate verification of clinical endpoints in studies based on parental responses to questionnaires. Until and unless these inconsistencies and inadequacies can be appropriately addressed and resolved, the available epidemiologic data do not justify a conclusion that there is even an association between parental or household smoking and adverse respiratory effects in children in this age group, let alone a relationship with ETS exposure.

REFE

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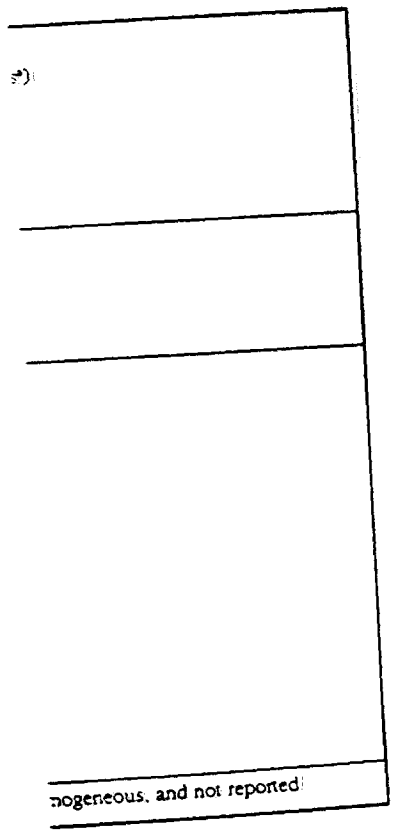

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